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OBJECTIVES OF MEDICAL EDUCATION

Leland S McKittrick, M D, Brookline, Mass

TO me the ultimate objective of medical education is to assure the American people of the best possible medical care To do this means (1) to carefully select and then to educate properly oriented, intelligent young people in the knowledge now available and to stimulate them to want to know more, (2) to continuously advance our knowledge of the prevention, cause, and treatment of disease, and (3) to train those we educate to apply what we now know to the sick patient and to develop incentives and methods of acquiring and applying new knowledge as it is developed

If our basic objective is to care for the health of our citizens, experience in the actual care of the sick is an essential part of our educational program We can assume that our medical schools equip their graduates with all of the scientific and theorectical knowledge that we currently possess But the hospital can give something absolutely essential to the patient care which is over and beyond the kind of education the school can give

The ability to interpret symptoms and to elicit and evaluate physical findings, the application of scientific methods and pertinent laboratory data to a sick person, the acquisition of certain technical details of various surgical procedures, and the ability to select the optimum time for surgical interference and the type of operation to perform on a critically ill patient can come only after hours of personal contact with, and responsibility for, sick people A relationship between the student and patient under the supervision of experienced clinicians which permits increasing experience in these factors, as well as an understanding of the behavior, the human needs, and the progress—not of abstract disease but of individual sick persons—is an essential component of every good program in medical education

It must not be forgotten, however, that each patient has a definite objective in coming to the hospital He wants to be helped He does not come primarily to help in the education of physicians Where there is a good educational program there should be good patient care, but this is not always so Generally, where there is good patient care there is a good educational program We, as clinicians and as teachers, must not forget our responsibility to these patients as well as to those whom we are teaching For both patient and student we must develop our teaching programs so that in our daily contacts with them we make every effort to share with each the tact, the discretion, the powers of explanation and persuasion, and the wisdom and warm human understanding that our years of patient care should have developed The rewards of experience are too valuable not to be shared Human life is a frail and precious possession Learning at the bedside or operating table should not come from trial and error but from maximum utilization of the experience of others toward the development of a pattern best suited to the individual student This concept of learning and gaining experience was brought to me one morning years ago

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Chairman Council on Medical Education and Hospitals American Medical Association
Chairman's Address read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 7 1960

while I was assisting the late Dr Daniel Fiske Jones He pointed out to me a certain technical detail in the course of what was then thought to be a difficult and hazardous operation and said, "Dr McKittrick, you will make mistakes as long as you practice surgery, but don't ever be guilty of making the same ones I have made Those you can learn from me"

If it is not already lost, we are in great danger of losing this concept of teaching Too much scientific orientation in heads of clinical departments, overemphasis on technique and disease, too much specialization within narrow fields with a tendency to focus on technical problems or a small segment of the body, and the concept that a good training program means early assumption of total responsibility not only in the treatment but in all decisions pertaining thereto are affording decreasing opportunity for the young clinician to profit by daily contact with and observation of, those who have learned the many aspects in a balanced relationship of the science and art of medicine from years of discerning experience

We hear much about service versus education, and we are concerned over the diminishing supply of ward patients in our teaching programs Too much service may mean too little education But too much emphasis on research and education may also result in a type of patient care which is impersonal and lacking in an understanding of the real needs of the patient

I am not apprehensive that our future teaching programs need be jeopardized by a lack of patients True, we may need a reorientation of some of our training programs, especially in surgery, but there will always be sick people who will come to our hospitals for help The proper orientation in the relationship between these patients and the student, the young physician, and the staff member may become of greater importance than it has been in the past However, if after the basic training of the preclinical years, emphasis is placed on understanding and fulfilling the needs of the sick and if each patient is looked on as a sick person in an atmosphere where student, intern, and staff physician work as a team in an effort to better understand and treat the patient (not where the disease process is studied and its course followed in a human being), where the desire to learn what is known and to inquire into the unknown, and where the will to teach and to help each other prevail, then you will have good medical care and good teaching Then you will always find patients to treat

1180 Beacon St

TRIBUTE TO DR. EDWARD L. TURNER

Leland S McKittrick, M D, Brookline, Mass

I would like to acknowledge my indebtedness to a man—a man with a mission to which he devoted himself in thought and in action throughout his working hours—an indebtedness which can now be repaid only by increased efforts in support of the principles for which he stood

I did not know Ed Turner until he came to the Council on Medical Education and Hospitals The breadth of his understanding of people and their needs, his knowledge of and devotion to medical education in its broadest sense, and the untiring and thoughtful application of an active, orderly, and imaginative mind to medicine's many problems, present and future, have been and will continue to be an inspiration to me for which I shall be forever grateful

Dr Vannevar Bush must have had such a man in mind when he described a cultured gentleman "He is a man who aspires to wisdom, because of his keen interest and broad knowledge of all that conditions his relations with his fellows and their relations with one another, who goes beyond this and strives to add to the sum total of human intellectual accomplishments and to establish thinking on a higher and broader plane He is a man who is modest and kind to the humble and unfortunate Above all, he is a man with a mission to minister to the welfare of the society in which he lives and who takes just pride in his guidance and his leadership He is a member of that select group upon which the continuance and further development of our free way of life intimately depends"

To all who are interested in medical education and its relationship to mankind, and especially to all of us who have enjoyed Dr Turner's confidence and have worked closely with him, his death is a tragic loss

I know of no place more fitting to pay tribute to Dr Edward Lewis Turner than here at a Congress on Medical Education and Licensure in which he was so interested and for which he did so much

1180 Beacon St

Chairman, Council on Medical Education and Hospitals

Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 7, 1960

MEDICAL SERVICE AS A MEDICAL SCHOOL FUNCTION

Arthur Richardson, M D , Atlanta, Ga

Perhaps the two greatest developments in American medical education in the past 50 years have been the acceptance of the basic sciences as the foundation of medical practice and the introduction of the student in his clinical years to the wards and outpatient clinics as a full-fledged member of the health team One of the major criteria applied by Abraham Flexner to the medical schools he evaluated in 1909 was the extent to which undergraduate students had access to patients Henry Pritchett in his introduction to The Flexner Report wrote "A hospital under complete educational control is as necessary to a medical school as is a laboratory of chemistry or pathology High grade teaching within a hospital introduces a most wholesome and beneficial influence into its routine" At that time only a handful of medical schools made use of bedside teaching while most resorted to demonstration of a few patients during didactic teaching sessions

Student Responsibility

Today it is a universally accepted fact that adequate clinical teaching can be accomplished only if the student is made to feel that he has a responsibility for his patient With the acceptance of this concept of medical education as the welding together of an accumulation of knowledge and the development of a sense of responsibility, medical schools have assumed a role of performing medical service What Pritchett and Flexner had to say about medical education in 1910 applies to an even greater degree 50 years later The only difference is one of degree While they conceived of facilities which could be found in or around a hospital, we are more apt to think today of a medical center which has a broader spectrum of functions Every modern medical school has been forced to assume a responsibility for an ever-widening degree of medical service Whether it is public or private, every medical school today is at least a quasipublic institution which must be sensitive to the health needs of the society it serves and from which it derives its sustenance

Medical Service

There is no denying that medical schools do engage in medical service as an integral part of their activities The real issue is which services and how much service they ought to offer Most of us have become tired of hearing a medical school compared to a stool with three legs, representing education, research, and service It is a poor analogy In these days of expanding research grants, we are inclined to forget that the single central function of a medical school is education It is possible for a school to have too much research and too much service The extent to which it engages in research and service should be governed first by the educational need and second by available resources If it is legitimate to compare a medical school to a stool we ought to see that the educational leg gets a little more attention than has been the case in recent years The starting point for any discussion such as this should be a clear definition of the aims and objectives of the educational program of each school Frequently in the past, schools have been established simply because clinical facilities were plentiful We have now had ample evidence to show that topnotch medical schools can be organized in areas of apparent limited clinical material The vital factor is not the number of available service beds but the density of population on which the school can draw Circumstances which are favorable to the development of a true academic environment are equally, if not more, important This usually means a close attachment to a university

In recent years a great deal of attention has been given to the cost of medical education While the method of approaching the problem from the financial position has been pretty well worked out, the over-all results have not been very illuminating to administrators of medical schools because of the widely varying circumstances under which the different schools operate Before such studies can have much meaning, medical educators must obtain at least an approximate answer to certain fundamental questions Given a student body of a certain size, how many teaching beds are needed to supply an adequate educational program for each service? What should the proper size of the outpatient clinic be? These are not easy questions to answer because a lot may depend on whether it is possible to fill each bed with the right patient at the right time

Answers to these questions are important if we are to determine how much service a medical school ought to perform and what resources it will need to provide a good education The lack of such answers has been the greatest stumbling block to working out relations between medical schools and charity hospitals in which undergraduate teaching is done When a medical school is given clinical responsibility which exceeds its resources it is

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Dean Emory University School of Medicine

Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 7 1960

generally the educational program which suffers first Under such circumstances there is a temptation for the faculty, which also constitutes the professional staff of the hospital, to solve its problems by giving too much responsibility and authority to students without adequate supervision

Members of the clinical faculty seem to feel that there is never quite enough clinical material for teaching, and they are reluctant to say what is enough It is significant that in a recent survey to determine how to increase the output of physicians, only a few medical schools felt they could conveniently increase the number of students in the first-year class, but most schools thought that they could accept additional students in the third and fourth years with little difficulty This can only mean that most schools are taking care of more patients than the bare minimum I must emphasize that I am not speaking against a school assuming responsibility for more patients than are needed for teaching I am making a plea for understanding so that schools are not expected to perform a pure service function without being given the resources to accomplish the job Fortunately in many situations this problem is now being recognized, and the local community is beginning to accept an obligation by making resources available for the excess service load

What has just been said applies particularly to those schools fortunate enough to have access to ample service beds in public hospitals Many schools are finding it necessary, however, to turn to private patients to obtain adequate teaching material Here again it is important to determine how much is needed for teaching, otherwise, a situation is apt to develop in which the nonmedical ool private physicians of the community will k on the medical school as an unfair competitor believe the first step in resolving the usual "town and gown" controversy is for the medical school to explain honestly and openly why full-time medical faculty must have some private practice and to explain the extent to which this may be expected to grow This cannot be done unless the schools have first thought through their needs for clinical teaching material

Another service which is placing a burden on the educational programs of medical schools is the training of paramedical personnel such as technicians, medical record librarians, and occupational therapists These training programs should be included in the environment of the medical school, however, they should be added without making additional resources necessary

Medical schools have a responsibility for one other service which they are just recently beginning to reorganize This is in the field of continuing education of practicing physicians This does not imply that all postgraduate education must be given by medical school faculty However, in the world in which we live medical education is a specialty It is the job for which faculty members are selected and in which they have had special experience Medical schools have a responsibility to society to make possible the means for every practicing physician to keep up with advances This is an indirect form of medical service

Summary

Medical service in the form of taking responsibility for the care of patients is a necessary function of the modern school in order to create the proper environment for the teaching of clinical medicine Careful studies are needed to determine the nature and extent of clinical facilities needed for a student body of a given size Where medical service exceeds that which can be justified for the educational program, resources other than educational funds must be available for taking care of the excess Otherwise the primary obligations of medical education may be compromised

Woodruff Memorial Building (22)

CARE OF THE PATIENT IN THE MEDICAL SCHOOL SETTING

Edmund D Pellegrino, M D, Lexington, Ky

Patient care and clinical teaching bear an integral and reciprocal relationship Each must be conducted at a level of excellence if the medical school and the teaching hospital are to fulfill their missions Yet, within this axiomatic statement, there lies a difficult and unresolved practical problem How can the goals and purposes of patient care and clinical teaching be made compatible and reenforcing, and how can each derive maximum advantage from the presence of the other?

The contribution of the medical school setting to the solution of this problem lies in the following three unique responsibilities (1) to provide that quality of patient care which can be a model to the student and a standard of reference for the community, (2) to refurbish this care continuously and keep it responsive to the needs of society, and (3) to keep abreast of useful knowledge in the natural and social sciences It is my purpose to ex

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Professor and Chairman, Department of Medicine, University of Kentucky College of Medicine

Read before the 56th Annual Congress on Medical Education and Licensure, Chicago, Feb 7, 1960

amine some aspects of the care of patients in the medical school setting in the light of these three responsibilities and their implications for student and patient

Clinical Education and the Teaching Hospital

The heart of clinical education lies in the introduction of the student to the patient under the catalyzing influence of the scientific and humane clinical teacher The aim of such education is fourfold to train the student's mind in scientific modes of thought as applied to clinical matters, to provide a fund of knowledge which this trained mind can use, to learn the techniques of clinical method, and to inculcate those values that are essential to the physician if he is to have a humble, compassionate, and responsible attitude when applying his knowledge to the problems of human beings A major concern is to effect a fusion of all aspects of our scientific and social knowledge of man with the lessons of experience and experiment and to temper all by the obligations of service

The physician s education should fulfill two requirements—the need for a comprehensive understanding of health and disease and the need to apply such knowledge to the prevention and relief of human ills It is to these ends that, in our times, the medical school works with the university on the one hand and the hospital on the other Thus, in addition to its traditional concerns, the university, by implication, takes on a responsibility for the provision of optimum patient care—patient care which must be a model for the student and a standard of reference for the community This unique feature of patient care in the medical school setting distinguishes it from good medical care in the nonteaching community hospital

Some Dissonances

The advantages of the association of school, hospital, and university in the complex organization of the modern medical center are great and clearly manifest in the achievements of contemporary medicine Yet, the chorus of praise for our present system of clinical education is not without some dissonances Indeed, few phases of the education of the physician are fraught with so much passionate controversy

Within medicine itself there are opposing views There are those who are exquisitely sensitive to the contributions of the physical and biological sciences to medical education and practice They rightly fear any change which might make medicine less critical, less exacting, and less inquiring On the other hand, others feel that clinical education is becoming too impersonal and too sharply focused on the details of disease and not enough on the patient It is said that the physician is being trained well enough technically but without regard to his role in society Suspicion afflicts both groups and is based on the fear that new ideas imply the loss of old values

These conflicts within medical education are symptomatic of something equally important—the divergent notions of the physician held by modern society He is often unrealistically exalted as a miracle worker who is technically flawless At the same time, there are serious misgivings about the way medicine is practiced and about the values that physicians have set for themselves Medical practice has been impugned as impersonal, fragmented, overspecialized, and insensitive to the needs of the community it serves Perhaps most regrettable of all has been the growing suggestion of deterioration in those ideals of service and kindness formerly supposed to have been hallmarks of the physician This divergence of opinions is no mere word battle There are real issues at stake which are pertinent to the care of patients and the basic education of the medical student

Need for Medicine to Evaluate Itself

Whatever may be the fundamental reasons for the misunderstanding between medicine and society, it becomes our responsibility, as physicians, to inquire into the possibility that some conflicting characteristics attributed to physicians have been nurtured in the teaching hospital in his formative years It is here, at a time when he is most impressionable, that the student is exposed to that quality of patient care which should be his standard of reference and the unfailing guide to the establishment of his values in his later education and practice

What is required if patient care in the teaching center is to serve as a model? How is patient care affected by the added dimension of teaching and research? What are its effects on the student, teacher, and, most importantly, the patient? Are there hidden defects in its apparent virtues? Does it include knowledge available from all sources? Is it current with and responsive to the needs of the society it serves?

It is wise to review such questions critically Although patient care is of high quality in the teaching hospital, the medical profession is continually required to make it better, for even small deviations can trouble the mind of the neophyte clinician It is axiomatic that the best patient care occurs where teaching and research flourish, but something may be gained if it is not assumed that the relationship is absolute Optimum care must be redefined in each age in terms of the knowledge and the needs peculiar to that age

Aspects of Patient Care in Teaching Hospital

Patients come to the teaching centers for essentially the same reasons that they enter other hospitals—the investigation or relief of symptoms and disability Few patients as yet consciously elect a teaching hospital so that they can participate in welfare of his patients remains unresolved. The student often perceives more acutely than his teacher the validity of nonphysician services for his patients. He is often dismayed, however, at the confusion of roles and the sometimes misdirected good intentions which he beholds in physicians, nurses, social workers, psychologists, and sociologists as they attempt to work out a modus vivendi. Since the clinician should be the final point of reference for his patient, he must understand the roles of other professional people. He must provide the thread of continuity, or the patient will surely become lost in the intricacies of "team" interplay. The student needs exposure to this interaction of disciplines, whatever field of medicine he concentrates on.

Importance of Control of Teaching Hospital

Abraham Flexner[2] emphasized the importance of control by the medical school of the quality of medical teaching as an essential to good education. The degree of this control is extremely variable both in kind and degree, as was emphasized by Dietrick and Berson[3] in their 1950 study. When such control is lacking, the medical school and the university cannot always provide optimum and comprehensive standards of patient care to which to expose its students. Contradiction may arise out of the supposed need for economic or organizational compromises between the ideal and the actual. One purpose of this control is to ensure that the medical school and the university can fulfill their unique obligations in patient care.

Reflections on the University Hospital

The university hospital is an ideal setting for good clinical education and patient care. As it is a relatively recent phenomenon it has many potentialities, as yet unfulfilled, which now present unsolved problems. In the future these will become actualities to improve still further the patient care and the kind of training that the medical student receives. While there are indications that improvements are possible and necessary in the way teaching is conducted and patient care is administered, we cannot impute to the teaching hospital all the deficiencies society seems to find intermingled with the excellencies of modern medicine. Some of the criticism can be directed back at society whose material values are most cogently exposed when personified in the physician. Though subject to social forces, the physician is a responsible person, and it is as a person that he is accountable for some of the misunderstanding.

Reflections on Role of Clinical Teacher

Goals of patients care and teaching can best be made to reinforce each other if teaching is organized around the care of patients. What may be needed is a more specific dedication of medical centers to this effort.

Some problems such as responsibility, service load, type of patient population, and relationship to community are in part approachable by changes in the organization of patient care, its physical setting, and its financing. Other and more subtle problems are dependent for solution on the attitudes, training, and interests of the clinical teacher. His central and catalytic position in the confrontation of student and patient is critical if patient care in the medical school setting is to fulfill its obligations. Some reorientation of his interests may be necessary.

Clinical faculties often do not understand why there should be a breach between their ideals and actions and the needs seen by society when medicine is now at the highest point of perfection in its history. It is a curious thing that the physician, so sensitively attuned to the needs of individual patients and so critical of his own abilities to measure up to them, is sometimes strangely and sadly deaf when these same needs are expressed by society as a whole.

Most of all, the clinical teacher needs to avoid the common human susceptibility to the elaboration of antinomies. To be scientific is not necessarily to derogate the social, cultural, and humane factors in disease, to be interested in service to patients and better ways to render it does not necessarily encourage "fuzzy" and unscientific thinking. Indeed, if such apparent contraindications are to be resolved, it is the scientific clinician alone who can do so. It is through his mind and action that those things pertinent to man in health and disease are finally filtered, selected, and focused for the benefit of the patient.

It is surely seeking the impossible and encouraging superficiality to ask one person to encompass all necessary knowledge and techniques. Yet the problem cannot be solved by denial of its existence. Clinicians with some of the interests that have been described are developing, and they should find their places on teaching services as leaven to colleagues and students. There is room for others who will proceed through the usual specialized training and who will see development of the integrative ability alluded to earlier as a legitimate goal of their scholarship. As the essence of science is in its method and not in the subject studied, do not all aspects of the clinical situation become valid grist for its mill—patient care included?

Another important deterrent to the clinician is the departmental organization of school and hospital. There is need for a definition of the common substratum of patient care so that present departmental lines can be easily transcended when they compromise the patient's needs for totality and continuity of care. Specialization can be regarded as a way and a technique of thinking about certain clinical problems, it need not express itself in separate organizational patterns. The advantages of departmental organization should be reviewed frequently to see whether they all may not be outweighed by the disadvantages or achievements in other ways.

Summary

Medicine must of necessity be responsive to the needs of society, for they are but the needs of persons multiplied and quantified Medicine can best work out a continuing redefinition of its aims in the university atmosphere The university hospital has emerged as the most appropriate place in which the synthesis of knowledge from many sources can be achieved for the good of mankind The way patient care is conducted within its walls becomes a real concern of the university Patient care in the medical school setting is unique as it must reconcile the needs of student and patient with maximum advantage to both

Patient care and teaching are indissolubly and reciprocally bound in the dimension of quality To compromise one is invariably to compromise the other Continuing reflection on both terms of this relationship is a special obligation of the teacher, the medical school, and the university

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THE PATIENT, THE PHYSICIAN-TEACHER, AND THE STUDENT

Robert C Dickson, M D, Halifax, Nova Scotia, Canada

The increasing complexity and scope of medical knowledge has led to general agreement that the medical student of today cannot be made proficient in even a large portion of the field of medicine It has, therefore, become the acknowledged aim of most medical schools to produce what has been variously termed the basic doctor or the undifferentiated doctor The aim of undergraduate education has come to be the provision of the broad knowledge which will permit the graduate to become, with further training, a good general practitioner, specialist, research worker, or teacher The aim is clear and not controversial The path to its achievement has been less clear and the subject of much experiment As a background it is of interest to consider briefly the development of the modern medical school as known in the United States and Canada and in doing so to consider the changing methods in the patient-teacher-student relationship

Ever since the Aesclepiadae began to observe and record the symptoms and natural history of disease, the patient has been the central figure in the teaching of clinical medicine The early teaching by the master-disciple method gave way to the Italian schools such as Padua where the student chose his teacher and largely planned his own course of study

The advance of basic science and preclinical science after the renaissance increased the complexity of teaching to the point where, by the early 19th century in Germany and Austria, both basic and preclinical sciences were considered essential to medical education and were taught by full-time teachers appointed by the university By the last quarter of the 19th century in Germany, the same control by the university existed in the clinical departments and full-time teachers were appointed who had graduate training not only in the practice of medicine but also in one or more of the basic or preclinical sciences

In Great Britain, the United States, and Canada, basic science and preclinical science departments with full-time teachers did not appear in medical schools until the last quarter of the 19th century Although Sir William Osler was appointed professor of medicine in the Johns Hopkins University and physician-in-chief to the Johns Hopkins Hospital in 1889, it was not until 1914 that he, with the heads of the surgical and pediatric departments, became a full-time professor (It would be redundant to enlarge on the importance of the contribution of Abraham Flexner to the development of medical schools on this continent)

Since 1914 the policy of appointing department heads on a full-time or geographic full-time basis has spread to most medical schools on this continent, particularly in departments of medicine The effect on the teaching in the clinical departments has been great and has not yet reached its maximum Osler, first as professor of medicine at McGill University and later at the Johns Hopkins University, stressed the correlation of pathology and clinical medicine His influence on Canadian medical teaching was profound

In 1918, Duncan Graham[1] became the first full-time professor of medicine in Canada Like Osler, he stressed the correlation of pathology with clinical medicine, but he also placed emphasis on the importance of understanding the physiological basis of symptoms and signs of disease His basic objective in teaching clinical medicine is expressed well in his own words taken from the eighth John Stewart Memorial Lecture read before the Dalhousie University Faculty of Medicine Annual Refresher Course in 1956 "Data gathered from the

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From the Department of Medicine Dalhousie University

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clinical history, the traditional methods of physical examination and the simpler routine laboratory tests are interpreted in the light of existing knowledge of the functions of the body and mind in health and disease and of underlying mechanisms causing signs and symptoms of disturbances of function in different organs and systems of the body"

Osler and Graham emphasized the importance of bedside teaching, and both were fitted by their training in preclinical and basic sciences to assist the student in the correlation of his knowledge of these sciences with the findings observed at the bedside They realized that the weakest link in medical education was the correlation of the preclinical sciences with teaching in the clinical departments This is still the most difficult problem faced by the medical school, and most changes in curricula in recent years have been stimulated by the desire to improve this situation Under such circumstances it is natural that different solutions to the problem would be tried in different schools

Teaching Program

In the hospitals the need for interdepartmental cooperation in the care of patients is becoming increasingly apparent but the traditional barriers between departments are difficult to break down, so this form of development is proceeding slowly in most hospitals It is understandable, then, that the integration of teaching between such departments has been slow and imperfect In some schools an attempt has been made to correlate preclinical science with clinical departments by means of symposiums in which a panel of teachers drawn from different departments presents the various aspects of the problem under discussion In other schools, the curriculum has been arranged so that the same broad subjects are presented simultaneously by various departments Both these methods have advantages and disadvantages which will be discussed later As a basis for discussion of this problem, one attempt at its solution which is in the process of evolution at Dalhousie University will be described

In considering this teaching program, it is important to keep in mind the objective of producing in four years a student who, with further training, is ready to develop as a general practitioner, a practitioner in a special branch of medicine or surgery, or a teacher and investigator in one of the preclinical or clinical departments To achieve this objective, the student must have a sound background in the basic and preclinical sciences In the clinical departments he must be taught the technique of examination of the patient in the broadest sense He must learn to interpret the collected data in terms of disturbed function of an organ or an organ system Only then is he in a position to decide what pathological process, what emotional disturbance, or more commonly what combination of the two could produce the disturbance found Such an approach leads to logical and complete diagnosis It demands the appraisal of the patient as a whole

It is evident that the main burden of such a form of teaching must fall on the department of medicine Other clinical departments can say at some stage in some patient's investigation that there is no problem for their specialty It remains for the physician to assume the responsibility for correlating all the accumulated data and, as it were, reassembling the patient after his diagnostic dissection The teaching in the Department of Medicine at Dalhousie is based on the view, which perhaps reflects the personality of the head of the department, that teaching time that does not involve genuine effort on the part of the student is largely wasted and that correlation between preclinical sciences and clinical medicine is best done at the bedside with some help from other means

First Two Years

In the first medical year a few patients are presented to the students, usually in theatre clinics in which a clinician and a member of one of the preclinical science departments collaborate in the presentation of patients whose problems clearly illustrate the application of the preclinical sciences to clinical medicine The purpose of such presentations is to show the student that the preclinical sciences have a very definite relation to clinical medicine and that they are essential to the practice of good clinical medicine They are intended to provide motivation rather than integration

The students' first true introduction to clinical medicine is in the second medical year in the form of bedside teaching of the examination of the patient by functional inquiry and physical examination At this time the student has not advanced to the stage where the history of present illness can be properly appreciated, but an opportunity is provided for the student to learn how to explore the function of various organs and organ systems by questioning the patient regarding symptoms and eliciting signs of disease by physical examination From the outset the teachers emphasize the pathophysiological basis of symptoms and signs By repeated practice, first on each other, then on patients in the hospital, the student acquires skill in the technique of physical examination, begins to learn how to take the patients' history, and, as he gains confidence, loses the awkwardness which all students feel at this stage of their development From the first the student is encouraged to attempt assessment of the patients personality and emotional status

The teachers chosen for this work are senior physicians with considerable experience and junior people full of enthusiasm Each student spends one-half of his time with a teacher of each type Undoubtedly this first introduction to the technique of examination is one of the most important parts of the medical student's education, and, while he must continue to perfect himself in this art for the rest of his life, the start given at this time is a most important one

While these classes in small groups are proceeding a course of lecture demonstrations is given, mostly by one man but occasionally augmented by physicians who have made certain fields of medicine their particular interest In these demonstrations, many patients are presented to the students to illustrate certain symptoms and physical signs, the emphasis on the physiological basis of symptoms and signs is again stressed, and their interpretation in terms of pathological processes or emotional disturbances is demonstrated

Third Year

In the third medical year, the student has advanced to the point where it is to be hoped he has overcome the initial awkwardness of his contact with the patient, he is now in a position to examine the patient as a whole It is argued by some that at this stage the student should enter on a clinical clerkship It is the feeling at Dalhousie that a student at this stage is not ready to make the most of a clerkship but requires closer supervision He has not yet acquired the knowledge of clinical medicine which must be obtained by diligent reading and by contact with patients throughout this difficult third medical year No matter how the curriculum is arranged, it appears that the third year of medicine is a difficult one, particularly in the field of internal medicine

While it is agreed that the student must read avidly during this year, some aid or guidance in his reading program has appeared desirable In the past in most medical schools on this continent, the lecture has formed the key method of providing this guidance, and at Dalhousie the lecture is still the favored form in some departments In the department of medicine, the lectures have been cut ruthlessly in order to provide time for more bedside teaching and for the development of what has been called the group tutorial The reason for this is threefold First, the lecture, as do other forms of didactic teaching, lends to the words of the teacher an authority which is rarely their due Second, it demands no contribution or effort on the part of the student beyond his ability to keep awake and perhaps write an occasional note Third, it does not stimulate thinking, except in the rare instance where a particularly gifted lecturer is able to arouse enthusiasm and thought among his listeners

In the group tutorial, as it is evolving at Dalhousie, the class is divided into groups of about 18, each of which constitutes a third of the class This group spends one and one-half hours discussing a previously designated subject with a teacher At first the teacher led a discussion based on the Socratic method of question and answer, with the teacher providing the questions In groups of 18 this did not permit as much student participation as was felt desirable, and a change was made whereby each class of 18 was divided into three groups who alternated in their roles each period One group of six, on a given day, asked the questions, a second group answered the questions, and the third group criticized both questions and answers At certain times the questions are poor and guidance from the mentor is necessary, but it is interesting to note that as the year goes on the students develop in their ability to ask questions and become interested in this form of studying a problem The method has gained steadily in popularity with both students and staff

It is hoped that this method of teaching will stimulate good reading habits, will counter the student's ingrained feeling that if he is ever asked a question on which he has not received a lecture he is being badly treated, will avoid the evil of the student regarding the spoken word of his teacher as gospel, and will encourage individual and critical thought From the teacher's point of view, it has the advantage that by the end of the third year he knows virtually all of the students well and some of them very well For the most part, the ones that are well known are in the top 25% and the bottom 10% of the class There are always a few in the middle who do not impress their personality on their teacher either favorably or unfavorably

The nature of the subjects chosen in these tutorials is such as to permit the placing of emphasis on the physiological, pathological, biochemical, and bacteriological bases for symptoms, signs, and disease processes All facets of the subject will not be covered as well by one teacher as they might be by another, although whenever possible teachers are given the material which they are most capable of handling However, it appears to be a sounder form of pedagogy for one teacher to attempt to correlate the preclinical sciences with clinical medicine than for the symposium form of teaching to be used Psychologically, the purpose is defeated if the student is asked to be able to correlate preclinical sciences with clinical medicine when it requires a team of four or five teachers to place this material before him 'How," says the student, 'am I supposed to be able to do alone what it requires four teachers to explain to me?"

It is apparent that the preclinical teacher cannot be expected to assume the responsibility for this correlation, but the clinical teacher, particularly the teacher of internal medicine, must be held responsible This emphasizes the importance of the principle recognized in Europe nearly 100 years ago that the clinical teacher should be exposed to the discipline of one or more of the preclinical sciences

The tutorial program is designed merely as an adjunct to the students study of sick people In the third year, he continues his bedside teaching in groups (six students with a clinical teacher) Time is provided for the student to examine one patient each week For this patient he takes a complete clinical history and performs a complete physical examination, he writes out the data in full and gives them to his teacher to be marked Some of these cases are discussed in detail with the group each week and emphasis is placed on the technique of examination and the interpretation of the collected data in terms of disturbed function Interpretation of the disturbance of function in terms of a pathological process, emotional disturbance, or a combination of the two is developed

Fourth Year

By the time the student reaches his fourth year, he is ready to profit from a clinical clerkship The weakness of this clerkship at Dalhousie has been the lack of supervision of the students This year an attempt to master this problem has been made by apprenticing each student to an individual physician who becomes his mentor The student is responsible for certain work on the wards of the hospital and in its outpatient department This is common to all students The individual physician-teacher, on the other hand, may adopt a different program from his colleague One may take his apprentice to his private office on one or more afternoons of the week Another may take him on ward rounds of his private patients or to visit different hospitals Still another may give reading assignments for further discussion Others will ask for the production of short theses It has been interesting to note the variety of approaches which the teachers have made The head of the department feels that the type of approach is irrelevant The important thing is that one student is the chief interest of one teacher who knows intimately what the activities of the student are and what progress he is making At the end of each term, the students are discussed and those who are weak are interviewed and helped to correct faults that have become evident It is too early in our experience to know how this project is going to develop, but the initial reactions of students and teachers are favorable

Review of the work in the third and fourth years and observation of the progress of the students has reinforced the view that a clinical clerkship in third year is premature To learn all the skills, methods of study and thinking, and the facts of clinical medicine alone, not to mention half a dozen other disciplines, cannot be done in one year instead of the present two years To try to make the fourth year an internship and the third a clinical clerkship would be, in my opinion, to push the student on too fast Even if the facts could be learned, the sense of confidence and judgment so essential to the doctor would not be developed as well as under a system such as that which has been described

It will be apparent that the methods of teaching internal medicine in the second, third, and fourth years are such that all demand effort on the part of the student and that methods of spoon feeding have been ruthlessly eliminated It is also evident that bedside teaching is the core of the whole plan This demands an adequate number of teaching beds in which the patients fully expect to be examined by the students In order to continue adequate bedside teaching, it seems essential that in teaching hospitals certain beds in a designated area be set aside for the teaching service This service must, of necessity, be under the direction of a physician appointed jointly by university and hospital and an adequate medical staff similarly appointed to work under his direction Patients admitted to this service would come under the care of the team consisting of student, intern, resident, and staff-physician The high standard of care which can be provided by such a teaching service will attract patients in more than adequate numbers even though widespread hospital insurance and prepaid medical care plans reduce the number of patients dependent on the old public ward system where the physicians' services were provided without charge

It has been mentioned that from the first contact with the patient the student is encouraged to try to assess the personality and emotional status of the patient In this he is aided by the teaching of a strong department of psychiatry It has been my experience that students today are well aware of the impact of the psyche on the soma but much less appreciative of the impact of the soma on the psyche Perhaps balance in this regard can be achieved only with experience, but it is another facet of medical education which can only really be taught at the bedside

A similar observation might be made in regard to the tremendous impact on the patient provided by sympathetic understanding, explanation, and reassurance based on sound knowledge of the patient's problem which was the outcome of adequate examination It is hoped that the apprenticeship introduced into the fourth year clinical clerkship will aid the student in acquiring an appreciation of this important aspect of medicine

The bulk of bedside teaching in Dalhousie and other (Canadian) medical schools is done by that dedicated group of physicians who are part-time teachers They bring to the bedside the personal touch which is rarely acquired other than in private practice For this reason it is important that a considerable proportion of teaching in the clinical departments should be done by such part-time teachers Some experience in the private practice of medicine is desirable in all clinical teachers, and geographical full-time appointments with limited consulting privileges are to be preferred to full-time appointments for any doctor conducting bedside teaching

As a part of the clerkship, the student spends a proportion of his time in the Outpatient Department Here he comes under the guidance of a few carefully selected general practitioners working under the direction of a senior member of the teaching staff In this atmosphere he learns to appreciate many of the socioeconomic factors which contribute to sickness He gains a knowledge of the people of the region and their mores, he begins to appreciate some of the simpler but perhaps more important factors which are spoken of rather loosely today as comprising the behavioral sciences

As yet no specific mention has been made of teaching the student about the doctor-patient relationship, compounded of interest, understanding, sympathy, firmness, and kindness, which arouse in the patient the feelings of confidence and hope which are so essential to good medical care No curriculum can assure that this will be taught well Rather, it depends on bringing student and patient together under skilled teachers who are also, to borrow a term from Dr Ronald Christie, professor of medicine at McGill University, 'good folk"

Conclusion

The words of Osler taken from an address entitled 'Teacher and Student delivered at the University of Minnesota in 1892 seem appropriate 'The inherent, vital element, which transcends all material interests, which give to a school glory and renown in their absence, and lacking which, all the pride, pomp and circumstance' are vain This vitalizing element, I say, lies in the men who work in its halls, and in the ideals which they cherish and teach"

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LEARNING THE PHYSICIAN-PATIENT RELATIONSHIP

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In October, 1959, the Association of American Medical Colleges (AAMC) held its second institute on clinical teaching, which was led by Dr Charles G Child III, chairman of the department of surgery at the University of Michigan As is usual in the planning stages of an institute, subcommittees found that they needed information to aid them in defining the nature and severity of problems suggested as topics for institute discussion Dr Herbert Gaskill and the members of his subcommittee, assigned to the topic "Science and Art in Teaching Responsibility for Patients, came to wonder on whose behalf they were struggling Both this subcommittee and the public seemed to feel that many physicians are either insensitive to the needs of their patients or deal with them inadequately

The subcommittee attempted to answer the following questions Does the young physician feel that he has a problem in this area? Wherein does he feel his medical education was deficient? Once the young physician begins to work regularly with patients, does he not quickly become skilled in his working relationships with them and is he not much more concerned about other lacks in his medical educational background? In any case, just how did the students who graduated from medical school before comprehensive care became a byword learn to work with patients?

To gain some insight into these questions, the AAMC research office queried graduates of the class of 1950 Presumably these graduates had been out of medical school long enough to have acquired some perspective regarding what they did or did not get out of medical school experiences, and, at the same time, their student days were recent enough for their experiences to be considered relevant to current medical educational programs Details of the mechanics of sample selection, questionnaire construction, and returns were given in the workbook for participants at the 1959 Teaching Institute[1]

Deficiencies in Instruction

Nearly 2,000 graduates from the 1950 class (a 75% return from a 50% random sample) responded to the questionnaire They were asked to choose from among four general areas of instruction the one in which their medical school experience had been most deficient Fourteen per cent of respondents were unable to make the choice and failed to answer the question Of those who replied to the question, 8% felt that their medical school experience had been most deficient in the basic medical sciences, 30% thought the deficiency was greatest in the teaching of application of the basic medical sciences to clinical problems, 20% were dissatisfied with the area of practical clinical experience, and 42%, by far the largest proportion, felt that their medical school experience had been most deficient with respect to practical instruction in the doctor-patient relationship Clearly, the typical medical school of the late 1940s was less adequate in teaching students how to work with patients than it was in at least three other areas of instruction

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of the educational process involved, are crucial considerations for future action

"If comprehensive care signifies humanitarian attitudes, faculty members may be selected to teach comprehensive care simply on the basis of their attitudes But if comprehensive care is to include a body of knowledge and a series of techniques, faculty members must be trained in this knowledge and these techniques or specialists in the behavioral sciences must be added to the medical faculty

In short, because of the pressure on the medical student for action directly related to removing the patient's disease, the clinic appears to be a poor place in which to introduce the student to the role of psychological and social factors in medicine

"If the above *conclusion is correct, it follows that* the student should be introduced to the role of psychological and social factors in disease prior to participating in the clinic Should this introduction take place in a basic course in the behavioral sciences in the already overcrowded medical school curriculum? The answer is obvious—if comprehensive care implies a knowledge of behavioral science, then medical students should learn behavioral science as a basic course And behavioral science, it should be pointed out, is not identical with psychiatry any more than clinical medicine is identical with biology But it must be recognized that it is an open question whether the behavioral sciences are, right now, developed to the extent that behavioral scientists are prepared to assume the responsibilities of a basic science course However, if this question is answered in the negative, it is difficult to see what the term comprehensive care can signify at this time, aside from denoting the endorsement of humanitarianism"[5]

The time is past for armchair discussion about whether the study of human behavior has a place in medicine, what can or cannot be taught, and who should teach The problems have been defined and a foundation laid on which future research can build That such research must adhere rigorously to the demands of scientific methodology is imperative

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THE PATIENT LOOKS AT THE MEDICAL SCHOOL HOSPITAL

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I still recall my first sortie into the operating room, when I was eight years old, and the lingering odor of ether mingled with the smell of sterilized drapes and steaming hot instruments which were being laid on a nearby table The surgeon, whom I had come to know quite well in the course of prior consultations, was no longer recognizable except for a voice from behind a white mask and the familiar steel-rimmed spectacles The worst came when they put the gas mask on, I had no air, and lights started to flash across my eyes in crazy eerie patterns accompanied by humming throbs The last coherent emotion was plain fear—fear that someone would start cutting before I was really asleep

Now there is nothing unique *in this* experience because it has been happening to people every day for years, but to each patient it is unique, this fact is occasionally forgotten, even at the better teaching hospitals, although significant strides have been made in handling this sort of problem, particularly in the realm of pediatrics[1] Patients entering a hospital are afraid in many different ways, regardless of how brave a front they may put up For some, the big decision has already been made when they resign themselves to separation from their normal home environment to enter the hospital, but fear and a sense of complete dependency exist in one form or another[2] fear of the unfamiliar, fear of being misunderstood, fear of the outcome, fear of pain and discomfort, and, more subtle than all the other kinds, fear of "bad news"

What does all of this have to do with the teaching hospital? I mention it only to introduce the idea that attention to this sort of thing along with other facets of the care and comfort of the patient must be the rule in a teaching hospital if medical students and house staff members are to develop into the kind

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of physicians whom we would like to have for ourselves and our families In this respect, it is encouraging to note Dr J Howard Means' belief that physician-patient relationships among house staff are much better now than they were 40 years ago[3] Moreover, although one might hope that each student admitted to medical school be brimming with the milk of human kindness, compassion, and understanding, it still helps if, while learning the science and art of medicine, the student can perceive these qualities as ever present in his preceptors and appreciate from the outset that they are indispensable to the practice of good medicine

It seems to be an obvious fact that patients, by and large, receive better medical care in a teaching hospital than in affiliated or nonteaching hospitals, for a variety of reasons Teaching exercises are more numerous, staff is selected from a more highly competitive group, there is more, and more extensive, research, and the very fact that teaching is taking place forces staff and students alike to be constantly on their toes The rotation of visiting and house staffs, the easy availability of consultations, and the continuous challenge of questions from all quarters cause many minds to bear on each patient's problem The patient cannot help but benefit There is no question about the advantages of being a patient in a teaching hospital, however, the question does arise as to whether this environment is optimum Despite its general excellence, there is room for improvement

The characteristics of the present-day teaching hospital are peculiar in that they can function either for the benefit or to the actual detriment of the patient I would like to discuss two of these characteristics, namely, ward rounds and diagnostic procedures, with emphasis on patients' reaction to them

Ward Rounds

Daily ward rounds constitute one of the most valuable teaching devices available to students and staff alike It is difficult to conceive of a teaching hospital without them On the other hand, there is too little recognition of the fact that rounds per se can be traumatic for the patient Almost 20 years ago Romano[4] published a study of the effect on the patient of so-called grand rounds, essentially an amphitheater type of presentation In detailed interviews with 100 patients before and after such sessions, he discovered no severe emotional trauma, but there were lesser, yet meaningful, reactions of which the medical staff was not always aware In fact, 24% of the patients were described as uneasy and tense' when told that they were to be examined, and they remained so during at least the initial part of the actual session A smaller number of patients were distressed at the account of their history because they learned details about themselves, e g, convulsions, of which they had been unaware, and there was a variety of other complaints or causes for annoyance Less than 50% gave evidence of having understood the discussion There was also considerable misinterpretation of many of the medical terms used

Others[5] have studied the effect of daily rounds involving examination of patients at the bedside This situation contains another variable, i e, the patients within earshot, which may compound the problem of misinformation and misconception as well as be a source of embarrassment to the patient under discussion if the presentation is indiscreet In these studies there seems to be general agreement that ward rounds are a source of emotional trauma to a varying number of patients and to a varying degree One author has gone so far as to implicate rounds as a precipitating cause of death in some patients hospitalized for myocardial infarction[5d] In another study, although most patients voiced no objection to bedside teaching, the staff nurses concurred that each ward round left a group of 'disturbed, anxious, and even miserable' patients[5c] Most of the studies cite the deleterious effects of certain ominous sounding words which are prone to cause misunderstanding or apprehension The less obvious include degenerative (misinterpreted as "degenerate"), failure,' "attack, prognosis,' "neurotic,' and 'coronary' Similarly, attempts to mask the history with such a phrase as ethanol intake' are not always successful After all, the patients who gave the original history in more prosaic terms are not misled for long by attempts to cloak a recognizable event in more abstruse phraseology, nor are their companions in adjoining beds, who are delighted to give their interpretation of rounds to the less informed patients

Despite these disadvantages, ward rounds usually have a salutary rather than a deleterious effect on the patients Most of the latter enjoy the moments of being the center of the stage They are comforted by the thought that a whole group of physicians is focusing attention on their particular problem But even these patients can have their moments of anxiety and doubt, and there should be a constant effort by the staff to reduce these sources of patient anxiety to the minimum The ability to do so depends primarily on the attending physician who conducts the rounds and secondarily on the house staff and students Obviously tact, understanding, and sympathy, which are components of the art of medicine, all play a part, and the degree to which the key figures on ward rounds possess these qualities determines the entire atmosphere Perhaps it is worth reemphasizing the monkey see, monkey do concept Clinical professors serve as role-models,"[5e] and their general attitudes and demeanour tend to become inculcated into the student's developing habits

Although no rigid code can be prescribed, the authors cited above seemed to agree on a few general points regarding ward rounds 1 The attending physician should be briefed about certain patients before rounds in order to guide the student through any delicate situations which may arise during presentation of the history 2 Many of the details of personal and social history, even though relevant to the patient's illness, are best discussed elsewhere and not at the bedside 3 As soon as possible after the examination of a patient, a member of the house staff should return to the bedside, answer any questions, clarify any misinterpretations, and, if necessary, translate what transpired in terms that the patient can understand This last point is too often ignored, which means that the anxious patient is often left for an unnecessarily long period of time to sweat it out by himself before he is able to get some reassurance 4 Bedside discussion of the "pros and cons" of various procedures has no obvious merit and, in most instances, is actually harmful Doubts about the value or the eventual outcome of the procedure are created in the patient's mind, and the net effect is to add unnecessarily to his burden of worry

Scientific Zeal

In any academic institution, the emphasis must certainly be on learning, on intellectual curiosity, on the scholarly pursuit of knowledge But when such an institution is fulfilling a service obligation, the service aspects and the academic aspects may compete and there is always danger of subordination of one to the other In the so-called nonteaching hospital, service aspects predominate and until recently have stifled the growth of an optimum academic atmosphere because of demands on staff time, organization, etc The more recent development of educational programs in a number of such hospitals is encouraging, and one hopes that Hill's[6] theory that every hospital should be a teaching hospital will be applied on a broad scale That the use of private patients presents no obstacle to the development of a first-rate teaching program has been convincingly demonstrated in an article by Dr Coggeshall[7] In the usual teaching hospital, however, academic philosophy is so well established that on occasions the patient as a human being is forgotten Certainly, this forgetfulness is not deliberate, nor does it last long, rather, it is a temporary oversight

First, all physicians have seen situations in which the patient's comfort is considered less important than an administrative routine Undoubtedly routines are necessary, but should they be so inviolable that they cannot take on other forms, particularly when change might serve the interests of hospital and patients alike? Staff members have to go off duty, laboratories have their hours, and an accurate diagnosis should be established as early as possible, but is it necessary, as happens not infrequently, for a patient to have three complete histories taken and three physical examinations performed in the span of 8 to 10 hours on the day of admission, particularly at a time when he is acutely ill? It would seem that perhaps one or two of these sessions might be postponed until the next day or, in certain circumstances, be eliminated entirely Another example is the annoying process of bloodletting Perhaps there is a therapeutic value, of which I am unaware, in numerous phlebotomies for diagnostic tests, but I am sure that the average patient would gladly settle for having them performed once rather than three or four times a day, particularly if the role of the leech is played by someone who is relatively inexperienced Some of these kinds of abuse may be blamed on poor organization and planning, but they fall into the same category as those resulting from excessively rigid adherence to a routine

Second, I think there is a tendency in a teaching hospital for the staff or students to propose many diagnostic procedures that may not be necessary, moreover, orders are sometimes written without sufficient thought as to what trauma, anxiety, discomfort, or, at times, even risk the given procedure may cause the patient Surely, it would be nice to have another bone marrow biopsy specimen taken, a residual urine determination, a gastric analysis, or a sigmoidoscopy But these things, if they do not actually hurt, are downright uncomfortable Do staff members always think of this when they order some procedure? How many have experienced the acute nausea accompanying the injection of contrast medium for intravenous pyelography? How many physicians have swallowed a stomach tube, have felt the gripes of a barium enema, have had bronchoscopy performed? It might be a good idea if all physicians underwent at least the simpler of these procedures so that they would know what they feel like In the long run the patients would undoubtedly benefit

There are two additional facets to this problem of diagnostic tests, one economic and the other educational Presumably the number of laboratory procedures carried out on patients with any given disease is now much greater than 20 years ago In the interests of good medicine and research it behooves today's physician to use all available means in order to arrive at an accurate diagnosis and to orient the value of therapy Certainly one would expect a larger number of procedures to be used in the wards, where, in most hospitals, the greater part of teaching is done This, in fact, has been shown by studies of Trussell and his colleagues[8] But it may be that many of the procedures involving laboratory and radiographic examinations are not really necessary and, indeed, cannot be justified within any of the three spheres of activity of a teaching hospital, namely, education, investigation, and patient care The extent of the abuse of laboratory procedures causes an economic burden which the hospitals, the patients, and the insurance organizations can ill afford Moreover, the indiscriminate use of laboratory tests defeats the educational objective of the teaching hospital The house officer who is permitted to order batteries of unselected tests as a routine or for the record or to play safe helps no one, least of all himself He loses the chance to develop critique and clinical acumen, and he learns bad medicine It is much easier to detect the omissions in the treatment of a patient than it is to crack down on a superfluity of procedures Nonetheless, a good teacher has an obligation to do both

Extra procedures carried out for research or teaching purposes are, of course, often valuable In many instances to state that such and such a reaction occurs is not enough, it must be demonstrated Moreover, a well-planned research project often requires many more tests than might be considered necessary for the care of the patient alone But here the benefits accrue to subsequent patients and are clearly justified It is not the sound use of laboratory tests that deserves criticism but their occasional abuse either by the scientist lacking compassion or by the humanist lacking scientific critique

Summary

The teaching hospital is an institution where patients can receive the best possible medical care The educational and investigative roles of such a hospital create a unique environment, the facets of which have a direct bearing on the patient's well-being Ward rounds, indispensable to the teaching program, involve certain hazards which can be minimized by a staff that is both considerate and alert Because of the increasing number of diagnostic procedures now available, it is necessary to resist the temptation to use them when they are unnecessary and to keep in mind the patients' comfort, the expense, and the interests of sound teaching The science of medicine and the art of medicine are complementary and are best fused into one phrase good medicine

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CLINICAL EDUCATION—A CONTINUUM

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A physician is usually an intelligent and highly trained person He is more than a brain The task of the medical educator is not to insert an arbitrary collection of medical courses into a selection of brains, it is to educate each student Osler says that the hardest part of the task is to convince the student that his education is not a medical course, but a life course ending in death, for which the work of a few years under teachers is but a preparation '[1] I would say that the task is made yet harder precisely because medical educators too frequently appear to act as if their aim was to cram the brain rather than to educate the person The student emerges from the process of being educated with a well-established pattern of behavior, whether the method used tends to cram the brain or to educate the whole man The pattern of behavior consists of the way the student has, by force of habit, come to use his skills and his knowledge as a scientist

Scientific and Clinical Method

The clinical program I am going to describe attempts to educate the scholar of medicine toward a

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specific end, the application of the scientific method to clinical practice The scholar must be shown that the clinical practice and the acquisition of knowledge in this area comes through the application of the scientific method to practice The use of this method in medicine is not new, for it was clearly outlined by Claude Bernard in his treatise on experimental medicine[2] The same approach has been successfully used to gain basic information in all scientific areas The method consists of the continuous application and reapplication of four fundamental steps stating the problem and studying it by means of observation, description, and classification, deducing the formulated theory and hypothesis, testing the theory or hypothesis, and revising and restating the problem These steps have their counterpart in the steps taken toward the solution of a clinical problem Such a problem is studied by means of a history, a physical examination, and basic laboratory tests, a tentative diagnosis is made, this diagnosis, or hypothesis, is tested by a clinical investigation, and the original impression and plans for treatment are revised Finally, the investigator reveals his findings to the patient and to his colleagues

A contrived pattern of behavior in clinical medicine requires the continuous use of these four steps in an orderly fashion Each physician has a basic responsibility for education, as does any other scientist He has a responsibility for the education of his colleagues as well as for the education of his patients As a medical educator the physician has as his first responsibility the definition of the ultimate goal of the process of education Second, he must delineate the methodology of this education These responsibilities are not such as to be safely assumed today and forgotten tomorrow From time to time the ultimate goal may need to be redefined, and there should be a continuous concern for and delineation of the respective phases in the program

A consciously contrived pattern of behavior should be followed from the beginning Throughout the process the objectives should be kept in mind and the past accomplishments should be integrated into those new objectives which follow in logical sequence as the novice is gradually transformed into the mature student of clinical medicine This continuum in education should begin in college and span the years of medical school, the period of house-staff training, and the later practice of medicine The early part should be under the guidance of a person skilled in the application of the scientific method, and the student should be encouraged to use this method

In a discussion of clinical education four things must be considered the theme, the environment, the participants, and the methodology

Theme—The theme of clinical teaching in medicine should be the solution of a patient's problem The student should be encouraged to become involved in the solution of this problem He should have the opportunity to proceed in depth rather than to cover a multitude of problems in a superficial manner This means that the student should be given opportunities to observe the patient during the acute phase of the illness and that he should be afforded time to follow the course of disease in his patient Some responsibility for helping to solve the problem by actively participating in its solution and some measure of emotional involvement in the problem quickens the student's learning

The problem should always provide the stimulus for learning The task of the teacher is to insure that the student be enabled to find over and over again his stimulus not in the presence or person of the teacher but in the problem to be solved Perhaps the most important responsibility of the teacher is to make sure that the necessary conditions exist to bring about this end If the teacher remains the sole stimulus for learning during the early years, there is no certainty about what will happen to the student's method of solving problems when he is faced with problems to be solved in subsequent, unsupervised programs The theme should be characterized by encouragement and education in the study of clinical problems in depth rather than by encyclopaedic gymnastics with esoteric information in multiple specialty and subspecialty fields

Environment—Throughout the ages the environment of clinical teaching has undergone many changes There have been shifts from bedside to classroom to laboratory and back to the bedside Osler, in his farewell address to American and Canadian students, said, "I desire no other epitaph than the statement that I taught medical students in the wards, as I regard this as by far the most useful and important work I have been called upon to do"[3] The wards are a necessary place for this teaching However, the breadth of this experience must be extended to meet the needs of the changing character of medical practice With increasing frequency physicians are called on to deal with chronic disease The area open for study must be extended to include all aspects of daily living, in the home, community, and place of work As in any line of investigation, the stimulus for these studies should come from the need to solve a specific problem and not from any curricular trend or instructional gadget Opportunity and freedom should exist to enable the student to find a logical solution to a patient's problem The student should learn to use the facilities of the community as freely as he uses the facilities of the hospital This freedom and these opportunities should exist at all levels of training

Laboratories should be adequate both to the service necessities of the institution and to the particular interest of the student These same laboratories should be available to the scholar so that he may pursue his interest Curiosity should be encouraged, and sufficient materials should be made available The student, the intern, and the resident should be supported in their exploration of their own particular lines of investigation

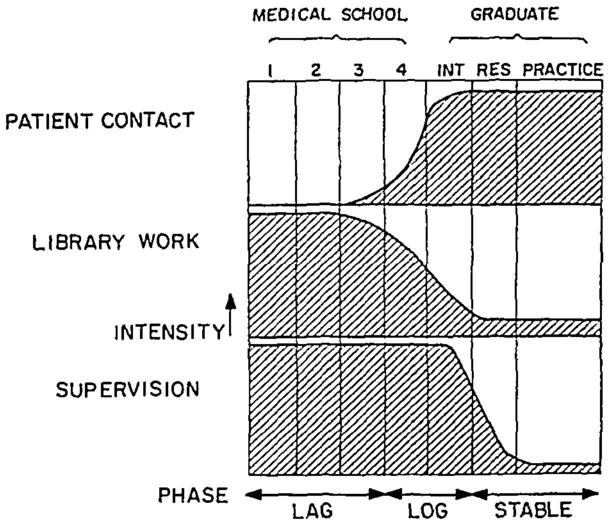
A library should be a part of this training environment The library should be conveniently located, adequately stocked, and policed only to the extent that a search for literature is not constantly frustrated by missing volumes which are inactively gathering dust in a doctor s office It would seem that the consideration of these needs should be a part of every hospital plan Apparently this is not the case Every day university and community hospitals are being built with no thought directed toward their service as potential institutions of learning

Participants—The three participants in the training program are the patient, the scholar, and the teacher The focal point is the patient Too much consideration and effort has been spent in defining a "good teaching case" Any person who feels he needs medical care constitutes the proper focus for the student of medicine and will serve as a good teaching case The student can profit by careful study of any such patient, whether the malady responsible for the patient's need is physical, psychological, or social Sufficient investigation usually reveals that all three forms of malady are present in each patient Every effort should be directed toward the quality rather than the quantity of patient contact

The scholar is the next most important participant in the learning situation Considerable study has been given recently to this element, but there are still many unknown factors [4] The desire to learn is the first and foremost attribute Early education should encourage curiosity and a healthy skepticism as well as provide adequate knowledge in the techniques of logic Moreover, the student should have the freedom to pursue problems in depth He should be comfortable with the uncertainties of the unknown It is important for future growth that the student learn early that there are no hard, cold facts, for it is obvious that the crass therapeutic credulity of the present generation does not stem from this type of healthy skepticism Finally, the student must be capable of accepting responsibility for the care and education of his patient

The teacher is the third participant involved in the clinical teaching situation The qualities outlined for the student are also needed by the preceptor In addition, he must have a real sense of joy and derive his greatest pleasure from the encouragement and observation of the productivity and development of his student The tutor must spend more time in encouragement of scholarly productivity and less time in impressing the student with the aura of staff infallibility Teachers who can bring forth from the novice in the group information which helps solve difficult clinical problems can do a great deal to motivate the novice to strive harder to become a thinker rather than a parrot This may also give the student the necessary confidence and encouragement The student should feel that he is a colleague, not an apprentice Medical schools are educating scholars and scientists not tradesmen

This method of teaching implies a constant search for ways to encourage the student to feel a responsibility for his own education Lectures have little place in this kind of teaching Bertrand Russell has said, 'Lectures as a means of instruction are traditional in universities and were no doubt useful before the invention of printing, but since that time have been out of date, as regards the abler kind of student" [5] Another important factor is that the teacher in a particular clinical situation can be the lowest man on the team, that is, he can himself be a student The student's uncontaminated viewpoint or his solution of a similar problem the previous day may place the mantle of leadership on his shoulders The good teacher recognizes this and encourages this approach It has been said that the difference between the faculty and students lies in the number of mistakes they have made, the members of the faculty have made more mistakes because they have been in clinical medicine for a longer time



Relative intensity of aspects of clinical training

Methodology—The figure shows a graphic representation of varying intensity of the three elements in the continuum of clinical training patient contact, library work, and supervision There is a gradual increase in patient contact, which reaches its peak during the internship As in bacterial growth, a considerable lag phase must exist, but this is not a phase of inactivity In this lag phase, there is an intense level of activity with each clinical contact For each contact there is considerable time spent with the patient and the instructor or supervisor and reading pertinent material in the library Time is included for the student to carry out the detailed education of the patient about his disease After this lag phase there is a phase of rapid growth There is a sharp decrease in supervision which, however, occurs at least one year after the increase in patient contacts, which gives one year of much contact with patients and much supervision

The internship is now the time when the student has the most contacts with patients and is under the greatest supervision Lack of supervision is one of the most frequent criticisms leveled at our internships today, according to a study of internships by Dr Gee[6] As the man goes into practice, supervision becomes minimal and is self-imposed through seeking the help of his peers

An Experimental Program

The program described in this section is the one used for clinical training at the University of Florida College of Medicine An effort is made toward this continuum with a cooperative effort of all clinical departments

Pre-Patient Training (First and Second Year)—The first course has been described elsewhere[7] The first-year courses, which constitute an introduction to medicine and are taught by a cooperative effort of the clinical departments, emphasize observation and the handling of statistics They are taught by university and medical faculty The students spend 4 hours observing various age groups in a laboratory school and 16 hours in detailed observations of one patient These observations are arranged in such a manner as to prevent interaction between observer and subject Hypotheses about behavior of each patient and a general theory of behavior are derived from such observations During the second year, the department of psychiatry teaches interaction of observer and subject and all clinical departments teach the techniques of medical observation, systemic pathology, and physical diagnosis

Patient Period (Third and Fourth Year)—In the third year, after mastery of the first stages of scientific investigation, involving observation, description, and classification, the student is brought face to face with the sum total of the clinical problems The basic clinical clerkship is designed to approach a clinical problem in depth and is a model for future clinical contacts The student does nothing except care for his patient and is assigned one patient a week Students do complete histories, physical examinations, and laboratory work on these patients There is sufficient time for exhaustive investigation at the bedside and in the laboratory Reading in the library is carried out with exercises on the use of the library when the student is dealing with clinical problems These efforts are carefully supervised, and the student presents his patients to a combined staff team consisting of physicians from many disciplines Here the student is taught a comprehensive approach to the patient rather than the limited, specialist's approach The objective at this time is for the student to master the basic approach to patients and their problems as well as to begin the process of learning from patients in a highly controlled environment, while being allowed sufficient time to do detailed studies The quality of contact is stressed, not the quantity Clerkships in psychiatry and in obstetrics and gynecology are also offered in the third year

The general clinic serves as an intake clinic and a clinic for continuous care All departments assist in the operation and teaching program, as they do in the basic clerkship For example, the psychiatry department has placed some of its long-term patients into this clinic and medicine has abandoned a general medical clinic Many of the specialty areas operate centripetally in that they send many of their patients to the general clinic

In the general clinic the same approach is applied to increasing numbers of patients The patients are not differentiated by disease or complaint The student has the opportunity to treat his patient for as long as two years, if indicated A woman with a normal pregnancy may be cared for until delivery, and patients with psychiatric or chronic illness may be treated for a year or more In this environment reading is encouraged and time for discussion with the professional staff is arranged The objective of this phase is to increase the pace of learning and, at the same time, to keep contact intense and comprehensive The outpatient contacts stress the environmental aspects of disease The student's treatment of each patient is graded Examinations are oral and deal with patients and diseases seen by the student A record of all student appointments with patients and performances are maintained in a central location

In the fourth year the final medical school effort is made the ward clerkship, where the frequency of contact is heightened but the thoroughness is still retained No effort is made to accomplish a comprehensive survey of the fields of medical specialization Patients are again the guide to curricular content No effort is made in the clerkships in medicine, surgery, or pediatrics to survey the field The student spends all his time on the clerkship He works intimately with the intern, resident, and staff member as a part of the team Records which give data on the types of patients seen by each student are available at all times through the statistical section of the medical record department. With this record system the experience of each student can be constantly monitored.

Internship (Fifth Year)—During the internship the scholar hits the rapid phase of clinical growth. He sees a rapidly increasing number of patients. The format of the patient investigation does not change, but the responsibility increases. The intern must have patients who are his own and, like the student, must have the opportunity to examine and to treat these patients over a long period of time. The amount of supervision must still remain great. This type of supervision is most difficult, for it must allow the intern the full opportunity to develop responsibility and initiative but also call his attention to his attributes and deficiencies. He learns to sort out quickly the expeditious lines of approach. These activities require judgment and the ability to decide quickly and accurately which observations warrant time and which can be passed over lightly. He loses the luxury of time permitted the student. At the end of this period of training the pattern is established as a reflex. Like the gyroscope of the automatic pilot with the airplane, these patterns keep the intern on course despite the buffetings of fatigue and other outside pressures.

There has been considerable discussion recently about elimination of the internship. This could be done in two ways, either by telescoping the fourth year and internship or by maintaining the same time relationships but starting the internship earlier in the clinical training. The first approach would be like trying to teach newborn babies to walk, the latter would be like starting the conception one year earlier. One cannot eliminate any part of any orderly growth process. It can be started earlier but must proceed in an orderly fashion. Unfortunately, at present the academic lock step prevents some from growing at a rate faster than the others. Any good program should take this into consideration.

Education for Practice (Sixth Year)—After the internship the scholar is ready to embark on education which is designed for special patterns pertinent to his choice of a type of practice. The intensity of patient contact must remain moderately high. Here for the first time the program should be directed toward practice rather than toward care of patients. If the student is interested in general practice, he needs to acquire special skills that allow him to assume the varied responsibilities which characterize family practice. If he is interested in specialty practice, he acquires other skills that allow him to work in a more limited area. If he chooses academic medicine, study in the basic sciences of medicine must be augmented by one to two years in a basic research laboratory. Thus, new objectives related to the needs other than those of a specific patient are introduced. In all three of these areas a curriculum should be planned to assure adequate exposure to the areas and supervision maintained at a level high enough to be certain that each student has proper contacts. The scholar now acquires special skills related to his practice needs. Here he must continue his basic pattern of behavior. During this period the economics and methodology of practice should be taught. The philosophy and methodology of internship and residency training do not differ from medical school training. The goals and objectives differ. It is in this area of training that the United States has woefully fallen short. Medical schools need another Abraham Flexner to awake them from their lethargy. The trade school residency training program must be abandoned.

Education in Practice.—Education after residency is the most difficult part of the continuum. The stimulus must come from the student. Problems of patients should remain the theme. Simple unoriented perusals of the literature and lectures in postgraduate courses are overrated as instruments of education at this period. One of the most effective means of education seems to be a review of basic and clinical literature pertinent to a particular problem of a patient. Presentation of such reviews to the colleagues and subsequent discussion increase the learning. In all years of clinical training the scholar should be encouraged to undertake investigation of fundamental laboratory and clinical processes. Each student should have contact with a research problem involving patient care. Scientific evaluation of his therapeutic efforts should be a part of this training. Clinical investigation should be going on around the scholar as he learns medicine, and the techniques should be stimulating enough to encourage him to continue critical studies, small though they may be, during his life as a physician. This investigation should continue through the internship and residency. All of these things can and should be a part of an internship and residency in either a medical school or a hospital not affiliated with a medical school.

Summary

Clinical education is an orderly continuum of increasing contact with patients, knowledge, responsibility, judgment, and skill. It is based on training in the application of the scientific method to the problem of a patient. The method is built around the solution of a problem. Two of the participants, the trainer and the trainee, work together as colleagues. The quality of the patient contact far outweighs the quantity.

By way of conclusion, I should like to quote a recent editorial "There is a real unifying thread that binds together the segments of medical education, beginning with the clinical clerkship in the third medical school year and running through the internship and residency programs "[8]

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DEVELOPING THE YOUNG PHYSICIAN'S RESPONSIBILITY AND JUDGMENT IN PATIENT CARE

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In the past few years, considerable attention has been devoted to the process of educating the medical student Endless discussions of this subject have occurred among the faculties of many medical schools, and a significant number of them have resulted in experiments in medical education that are being observed with great interest Conferences, such as those sponsored by the Association of American Medical Colleges, have taken place with increasing frequency Sporadic efforts are being made to accumulate, in a scientific fashion, data that will provide a more lucid comprehension of the many factors that influence beneficially or adversely the intellectual maturation of the medical student

During this past decade of enlightened and praiseworthy experimentation in undergraduate medical education, efforts to study and improve the graduate education of the physician have been negligible Occasional studies by individual departmental directors have been conducted but have not been publicized widely It is apparent that the exhausting efforts of medical faculties to improve undergraduate medical education have diverted, at least in certain instances, the attention of clinical teachers from the problems of graduate education This has been unfortunate When the faculties of medical schools accept the same enthusiastic responsibility for graduate education that they have accepted for undergraduate education, significant advances and improvements in the education of a physician are inevitable The universities in this complex and rapidly evolving society are the only institutions that can logically provide the qualitative standards and professional guidance for the education of the graduate physician Until such time, clinical directors will establish individual patterns and standards of graduate education as they have done ever since a physician first assumed the responsibility for educating an apprentice

The author's experience in graduate education has been in the field of surgery Educating a young physician for the practice of medicine in any of the specialties, however, involves the same principles that apply to graduate education in surgery The over-all objectives of a residency program are to develop a physician or surgeon who has a sympathetic understanding of the patient's total problem, who is cognizant of his moral and ethical responsibilities to patients and colleagues, who has acquired considerable knowledge of the pathology, pathophysiology, and natural history of disease, who has the capacity to analyze data critically, who has developed good clinical judgment, who has acquired precision in technical performance, and who is dissatisfied with his present comprehension of biological science and methods of therapy to the point where he will constantly have an inquiring attitude toward new information and will attempt to improve himself

There are many factors that must be integrated into a program for educating interns and residents if they are to have responsibility and develop judgment in the management of their patients Many educators would agree that the graduate physician

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learns most rapidly and effectively if he is in an educational environment that permits him to mature intellectually and professionally by accepting progressively more responsibility for patient care An elaboration of the following factors will lead to a comprehension of the phrase "educational environment

Motivation

The first determining factor is the motivation of the intern or resident In general, this is no great problem for the educator The physician with a recently acquired M D degree, irrespective of his ultimate objectives, is one of the most highly motivated young men in our society This is particularly apparent when he has selected the specific field of medical practice that he intends to follow throughout life The intern, who at the time of graduation from medical school is already convinced that he wishes to be a surgeon and selects a straight surgical internship, displays invariably a greater drive and initiative for learning than does the rotating intern who either has not decided upon a career in a specialty or rotates through services in which he has little interest

The educator s appreciation of the strong motivation characteristic of the graduate physician should make him aware constantly of the need for maintaining the intensity of the motivation by presenting the graduate with progressively more difficult intellectual challenges and rewarding him in a variety of ways for accomplishments already attained The fact that the educator will recognize the successful discharge of a responsibility to be assumed by the graduate is a stimulus for growth The appreciation by the resident of his own ability to solve a clinical problem and conduct a successful course of therapy is a stimulating and rewarding experience The ready availability of the clinical teacher to the graduate physician for counsel, advice, and, on occasion, assistance in the management of the patient is the essence of a supervised teaching program The initiative, however, must reside with the intern or resident Fear of reprisal for mistakes committed has no place in this educational process as it promotes stereotyped thinking and inhibits spontaneous motivation for learning

Patients

A second important factor for the development of responsibility and judgment in the graduate physician is the availability of patients for whom he can assume responsibility under a type of supervision to be described subsequently The patients optimally should exhibit a wide variety of disorders so that the graduate's perspective of his field will be broad For instance, the general surgeon during his graduate period should work temporarily in all fields of surgical activity, with the possible exception of ophthalmology Although he may practice ultimately in a restricted field, he will have better perspective and improved judgment by virtue of his exposure to the fields of neurosurgery, urology, orthopedics, otolaryngology, gynecology, and thoracic, plastic, and pediatric surgery

It is more important that the surgical specialist have an extensive background in the field of general surgery before his graduate education in the specialty commences if he is to attain a broad perspective and develop a high quality of judgment for patient care An adequate distribution of patients with ordinary, unusual, and emergency problems must be available A most important prerequisite for the development of responsibility and judgment by a graduate surgeon is the necessity for his assuming the responsibility for the surgical problem presented by the patient and for all aspects of the patient's care A knowledge of associated chronic renal, cardiovascular, respiratory, and hepatic disorders will develop a more mature judgment when decisions about acute surgical problems have to be made Consultation and advice from other services are of considerable value to the surgical resident in this learning process, but only if he has the ultimate responsibility for the care of the patient while he is on a surgical service

No simple or single solution for the diminishing number of ward patients is available A change in the character of medical practice within teaching hospitals that wish to preserve services for educational purposes is probably essential Since the indigent patient is rapidly disappearing, a new economic classification of patients admitted to inpatient services will be required This will raise many questions and objections from county, state, and national organizations Organized medicine, however, has as great a stake in the maintenance and improvement of educational standards for the graduate physician as do the educators The public has an even greater stake in this problem A change in the economic classification of inpatients or outpatients is, to a certain extent, in competition with physicians engaged primarily in the practice of medicine Other adjuncts, such as the affiliation of teaching hospitals with municipal, county, state, or federal hospitals, will help to preserve the services wherein maximum responsibility may be provided for the graduate physician This type of affiliation, however, can not be the sole means of providing a teaching service, as most institutions of this sort have a patient population that is highly restricted with respect to age, sex, or type of disease

Much has been written in the past few years about the diminishing number of ward patients The increasing loss of ward patients has already affected seriously the quality of graduate teaching in many hospitals in this country If ward or teaching services become extinct, the opportunity to provide the graduate physician with patients from whom he can learn by accepting responsibility for care will no longer exist, and the quality of teaching programs will decrease precipitously The next generation of physicians will have to learn the practice of medicine by following the examples and patterns established by others This type of activity can be classified as training, not education Training denotes the development of an ability to perform one or more acts, but it is not associated necessarily with the development of any judgment that indicates when, where, or how the acts should be performed in the best interests of the patient The term graduate training is applied commonly to the postdoctoral education of a physician It is, however, a gross distortion of the truth to use the word "training" when reference is being made to the education of a physician Seals and other dumb animals may be trained to perform entertaining and sometimes useful acts Physicians, however, should be educated The mere substitution of the word "education' for "training" denotes a more complex process and perhaps would inspire those engaged in the education of graduate physicians with a keener appreciation of the obligations of their position

Standards of Performance

A third factor in developing an educational program for graduates is the establishment of standards of performance This has little to do with the development of judgment, but it plays an important role in the ultimate responsibility that the graduate will feel for his patient This quality of a sense of responsibility for the patient is highly developed in physicians Fortunately, this quality is an inherent characteristic of most people who take up medicine as a career It can, however, be modified unfavorably by the daily observation of teachers or members of the staff who are dilettante and indifferent to minor needs of the patient, who use more art or rationalization and less science in their practice, who accept responsibilities for which they are not qualified, or who refuse to accept unpleasant responsibilities that might adversely affect their professional reputation

Teaching Staff

The fourth factor, and perhaps the most important, is the attitude and conduct of the teaching staff The members of the staff must be imbued constantly with the fact that their objective as teachers is to provide an optimum opportunity for the resident to use his own initiative to learn the practice of medicine To a great extent, this attitude will depend on how the director of the service conducts himself in all of his activities The manner in which he takes care of his own patients, the fashion in which he conducts either formal or informal teaching conferences, the interest that he displays in research, his knowledge of the history of his field and the current literature in it, the frankness with which he discusses his own errors in judgment or technical faults, and the humility with which he recognizes his own ignorance all make a lasting impression upon the graduate physician and establish to a great extent the pattern which other members of the teaching staff will display toward patient care, teaching, and research

The director of a teaching program, or any member of his staff, who indulges in tyrannical autocracy or demagogic pedagogy is doing his utmost to inhibit spontaneous motivation for learning on the part of his residents Frequently, staff members feel that they are teaching when they impart their wisdom and experience to the novice, whereas they are only being teachers, in the true sense of the word, if they guide the residents in the rationalization of a problem and the induction of a logical conclusion that is consistent with their experience and wisdom A spirit of inquiry must be maintained constantly in a graduate teaching program This applies not only to the daily care of patients but also to the promotion of clinical and laboratory research as opportunities and facilities may be available All members of a teaching staff should support this attitude of inquiry and all should be engaged in some type of investigative work Facts concerning disease and therapy are changing too rapidly for any teaching staff to be satisfied with what they learned yesterday or even today

It is easy to make definitive decisions about the care of a patient and to carry out the various procedures necessary to restore the patient to his previous state of health, but if this is all that the teaching staff desires the resident to understand, then a serious defect in the program exists The resident must be impressed with the need for comprehending how these decisions were arrived at logically, all of the biological scientific data that is known concerning the pathogenesis of the disease, and the effect of the therapy on the disease and the patient If there is some knowledge or information that the resident is lacking and that is required for a satisfactory comprehension of the patient's problem, it is more worthwhile for him to make the effort to obtain this information than to have it merely transmitted from the teacher When controversies concerning patient care arise, the resident must have the opportunity to examine both sides and arrive at a conclusion that appears logical to him This may be tempered ultimately by the decision of the teacher who has had more experience, but any suppression of the resident's opportunity to arrive at his own conclusion, based upon his experience and inductive powers, must be avoided

The extensive growth of full time teaching staffs in university hospitals and the fairly recent introduction in significant numbers of directors of medical education in nonuniversity hospitals have significantly improved graduate education Unless at least one person on a teaching service has as his primary responsibility the organization and conduct of the teaching program, the resident staff will be of secondary interest to the physicians attempting to conduct a teaching program as a secondary obligation This is true in spite of their avowed devotion and dedication to the operation of a residency program Educating a group of young physicians for the practice of medicine is a dynamic process that requires considerable thought and energy each day Success can not be obtained optimally by physicians whose interest and energy are devoted primarily to the practice of medicine

Supervision of a graduate program denotes a variety of attitudes and activities that are designed for the best interests of the residents learning experience and not for the convenience of the teaching staff Members of the teaching staff must be readily available for informal consultation by the residents at all times The teacher must be willing and able to spend a sufficient amount of time with the resident, discussing any particular patient's problem This signifies that the resident feels free to open this discussion with the attending physician or surgeon in the nurses' station, the hallway, the locker room, or the parking lot The best teaching by a devoted staff is carried out in this fashion rather than through formal teaching conferences

As a corollary of the preceding discussion, the director of a service or the person responsible for the educational program must have the freedom to appoint to his teaching staff only those physicians who are capable teachers and are willing to devote sufficient time to their teaching activities He must also have the same freedom to remove from the staff any person who fails to fulfill his teaching responsibilities

The teaching conferences for graduate physicians, some or most of which should be conducted by the director of the service, should be organized in a way that maximum participation by the resident staff is possible The quality of the teaching conference to a great extent depends on the time and effort used by the residents in preparation for it The teacher conducting the conference must constantly use every device at his disposal to have the members of the resident staff think and express themselves When there is disagreement among them, the residents must be permitted to exploit their theses to the fullest If a logical conclusion cannot be obtained with the information and knowledge that they have available, they must be given the opportunity to secure additional information and to continue the discussion at another time The mere recitation of the events that took place during a patient's hospitalization that may have terminated in either discharge or death can be a useless process unless the teacher leads the residents into a discussion of how and why the events took place In this manner judgment is developed

In an open teaching conference, errors in judgment and technique must be brought frankly into the discussion Personal criticism should be avoided as nothing is gained by it and it can do a considerable amount of harm by suppressing individual initiative The freedom with which a resident brings his errors to a teaching conference without fear of personal chastisement is the best motivation for the avoidance of similar errors in the future

The physician conducting a teaching conference should avoid pointedly asking junior residents of the staff questions that they are incapable of answering satisfactorily This embarrasses the young man in the presence of the senior residents It will inhibit his freedom of thought and will arouse in him a resentment for being placed in such a position Separate teaching conferences for the junior members of the resident staff who are at about the same stage of professional development are desirable, just as they are for medical students

Interns and residents who apply to a teaching hospital for their graduate education must be impressed with the fact that, as their knowledge and experience increase, they have a responsibility for teaching junior members of the resident staff, nurses, and, in some instances, medical students Teaching assignments of this nature play an important role in developing the resident's awareness of his Hippocratic responsibility for the progressive transmission of knowledge

Summary

An organized educational program is required for interns and residents if they are to mature intellectually and grow professionally as rapidly as possible Direction by a person whose principal interest is the education of the resident staff is necessary, in addition to the devotion of all members of the staff The essential factors in the creation of a proper educational environment are (1) the selection of highly and properly motivated graduates, (2) the availability of patients for whom the residents can assume responsibility, (3) the establishment of high standards of performance, (4) and the attitudes and activities of the teaching staff with respect to teaching, research, and patient care In such an educational environment responsibility and judgment are developed most effectively

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EFFECT OF HOUSE STAFF TRAINING PROGRAMS ON PATIENT CARE

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The effect of house staff training programs on patient care has received relatively little formal attention The few observations which have been recorded lack acceptable controls It would be desirable, for example, to use as a standard the level of patient care in a hospital which has no house staff I have never worked in such a hospital, and in the present circumstances I find this a handicap My assignment is further complicated by the almost endless number of variables that have to be taken into account Interns and residents, even those with the highest intellectual attainments, do not possess characters cast in a common mold Regardless of the training program and technical skills, the house officer's perceptiveness and the impact of his personality on that of the sick person are likely to determine whether he will have a favorable or unfavorable effect on the care of the patient

At one end of the doctor-patient interchange there is this variability of the house staff, and at the other end there is the even greater variability of the patient Patients do not possess the knowledge required for an evaluation of the house officer's professional abilities, and they may overrate or underrate his contributions to their care I can look back on a number of occasions when I learned to my surprise that the intern whom I considered to be the least able member of his group was regarded by many of the patients to be the one indispensable member of the staff In assessing the effect of the training programs, what weight are we to give to the patient's uninformed but certainly not unimportant evaluation of the care which he receives?

My association with interns and residents began in a large university hospital After some 20 years there, I moved in 1947 to a small general hospital in a relatively inaccessible farming area in upstate New York I shall not, however, reflect the experience and attitudes prevailing in a typical community hospital The village in which the hospital is located, once famous as the home of James Fenimore Cooper but now acclaimed as the birthplace of baseball, is a quiet, unaggressive town which after a century and one-half of growth has not yet attained a population of 3,000 In spite of the small population, the village hospital has a staff of 10 interns and residency training programs in five major specialties It is, therefore, no ordinary rural hospital We think of it as a miniature university hospital situated 200 miles from the university with which it is affiliated

Our internships are popular We have a large group of applicants each year, and our quota is regularly filled by the matching machine I take this to mean that the students have a high estimate of the educational value of our internships Now I have some reason to believe that if our patients were selected by the same type of matching process, we might not fare so well This is because there are some incompatabilities between the best training program for house staff and the best program of patient care, insofar as they can be judged by the patient who is involved in the process These incompatabilities arise because the suffering, anxious patient cannot detach himself from his predicament in order to take the long-term view When he is well he recognizes that the doctor of tomorrow has to be trained in today's hospital, but when he is ill he has no great enthusiasm for being fitted into the program of instruction Training programs must be appraised from the point of view of both their long-term and their short-term effects on patient care

It would be an act of supererogation to argue that house staff training produces better practitioners of medicine No one disputes this fact Such training is universally acknowledged as an indispensable foundation for the practice of surgery, internal medicine, and many other specialties The long-term effect of house staff training on patient care is undoubtedly favorable

Objections to some of the short-term effects of the actual training process have gained impetus as the economic, educational, and social status of the average patient has changed in recent years The patient paying the bill has a right to know what he is paying for, and we must be prepared to give him a reasonable explanation of the advantages he has when he is treated in a hospital which has a house staff In my experience patients who are made aware of the advantages become extraordinarily tolerant of the annoyances which seem built into the system

Criticisms of Training Programs

I propose now to enumerate and discuss some objections to the training programs, which have come chiefly from patients themselves In our area of New York, the area of the Utica Blue Cross Plan, there are 32 hospitals Ours is the only one of these hospitals which has interns and residents Our patients have frequently been hospitalized in at least one of the other hospitals of the area They are therefore in a somewhat better position than I

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to compare the medical care which is offered in the two types of hospitals In many instances they seem to find the comparison a favorable one for us, but I shall enumerate only the unfavorable criticisms

Duplication —Some patients complain of the annoyance of having multiple examinations and of being asked the same questions repeatedly Our answer to this criticism is that duplication and repetition afford protection to the patient There can be no doubt, however, that this is one field of accounting in which a credit may, by simple multiplication, be converted into a debit Therefore, in addition to justifying a reasonable degree of duplication, we must endeavor to keep unnecessary duplication to a minimum

Ward Rounds—Some patients complain that ward rounds upset them and make them nervous Two recent studies of patients attitudes toward ward rounds, one carried out at the Mt Sinai Hospital in New York [1] and the other at the Boston City Hospital,[2] led to the conclusion that most patients do not object to ward rounds and that some actually derive reassurance from being accorded this special attention On the other hand, there are a few to whom the experience is an unwelcome ordeal Both studies suggested that the adverse effects could be minimized if the patient were prepared for rounds ahead of time, were protected from careless and disturbing remarks during rounds, and were given an explanation of results and an opportunity to ask questions after rounds Kaufman and associates [1] suggested ways in which rounds might be used to produce positive rather than negative therapeutic results

Impersonal Attitudes—Some patients complain that the house staff pay little attention to the sick person's peculiar problems This is the same sort of complaint which we have seen recently in some sections of the public press that patients are looked on as mere numbers or filing cards, as interesting or perhaps uninteresting examples of disease, rather than as suffering human beings with a multitude of anxieties and social problems Although our training programs should be, and frequently are, designed to eradicate as far as possible this impersonal attitude toward patients, I fear that we sometimes leave ourselves open to the charge of professional arrogance

Accent on Longevity—Closely related to the foregoing subject is another trend which probably has more farreaching implications Several months ago, at the dedication of the new medical center in Palo Alto, Mr William McPeak, vice-president of the Ford Foundation, expressed his conviction [3] that without realizing it we have begun to be preoccupied with the security and length of old age—with the quantity of life more than the quality of living" This is a cogent observation and has bearing on our house staff training programs

For several years I have been troubled about our steadily growing ability to promote longevity Antibiotics and other new drugs, new surgical operations, mechanical respirators, artificial kidneys, and extracorporeal hearts and lungs have all contributed in a marvelous way to the advancement of patient care I have no doubt that in the years ahead there will be more lifesaving wonder drugs and more and better designed apparatus to take over the function of vital organs No one would want to decry such progress, but we must be on our guard against the appalling consequences of its perversion

It requires no particular exercise of the imagination to visualize a hospital 50 years or perhaps only 20 or 25 years from now with more than half of its beds filled with elderly patients who have lost forever the capacity to enjoy living, in fact, many of them may be totally unconscious of being alive We can see the dim outline of this picture in our hospitals today All too often it is looked on as part of the triumphal progress of medicine, but prospective patients and their families are becoming skeptical, even fearful, of these quantitative victories No one wants to celebrate victories which can result only in untold anguish to the patient and his friends, insupportable financial burdens for family and community, the diversion of medical resources from those who could use them more effectively, and a great increase in the cost of hospitalization for the average patient

This problem is one of the toughest issues with which medicine of the future will have to concern itself The medical, economic, and social aspects are formidable enough, but in addition one becomes involved in ethical, moral, and religious precepts with which we have no license to deal Three centuries ago, Sir Thomas Browne, discussing some of these issues in his *Religio Medici*, said, Were I of Caesar's religion, I should be of his desires, and wish rather to go off at one blow than to be sawed in pieces by the grating torture of a disease There is but one comfort left, that, though it be in the power of the weakest arm to take away life, it is not in the strongest to deprive us of death [4] Today, even the weakest arm, unless restrained by a stronger, is sometimes capable of withholding for weeks or months that one comfort

I need not emphasize the bearing that this fact has on the house officers role in patient care I would like to make the house staff realize that they would not be shirking their responsibilities if some of the time and energy which they now feel compelled to spend in the cause of fruitless longevity were to be devoted to the promotion of factors which make it possible for their doomed patients to live in peace and comfort and for their surviving patients to live more abundantly I do not use this expression in the familiar, quantitative sense but in the qualitative sense in which it was originally used in the New Testament "The thief cometh not, but for to steal, and to kill, and to destroy. I am come that they might have life, and that they might have it more abundantly" (John 10:10).

Responsibility.—Some patients complain that too much responsibility is delegated to the house staff. We have to take care that the amount of responsibility assumed does not exceed that actually delegated. Responsibility is essential to training, and, if properly regulated, it need rarely come into conflict with the best interests of the patient.[5] When such a conflict exists, it must of course be resolved in favor of the patient.

Underrating the House Staff.—Some patients refuse to accept advice from the house staff or to submit to diagnostic or therapeutic procedures unless they are performed by a senior physician. This attitude, which may defeat the best-laid plans for the care of the patient, can usually be dispelled if someone in authority will take the time to tell the patient about the status of the house staff and its important role in modern medical care.

Overrating the House Staff.—Some patients overrate rather than underrate the status and abilities of the house staff. A patient may become so dependent on a particular intern or resident that his treatment is undermined when this house officer, in the course of normal rotation, is shifted to another ward or service. In some instances the patient's dependence on a house officer results in weakening the effectiveness of the family physician. The house staff should be made aware of these dangers and should be told how to guard against them. Nothing can have a more devastating effect on the long-term care of the patient than having his faith in his home physician shaken.

Who is my Doctor?—The sheer size of the medical team resulting from the presence of a house staff is baffling to some patients. If there are too many voices of authority or if it is not clear to the patient that his vital interests are being governed by someone who is competent, sympathetic, and approachable, confusion and insecurity will result. We try to prevent such confusion in two ways, by distributing to each patient prior to admission a booklet describing the medical staff and other hospital personnel and by including a description of the staff in the regular duties to be performed by the intern when he greets his newly admitted patients. Some of the more important contributions will now be described.

Most of these criticisms of the house staff came from medically unsophisticated patients. Before reaching the ears of the staff they may have been passed about the community from person to person. In the repetition they may be built up to very formidable proportions. It is noteworthy that none of the criticisms raises any question about the technical skill or the professional competence of the house officer. They arise for the most part from annoyances or from a lack of understanding of the status of the interns and residents and of the very real contributions (described below) which they make to the care of the patient.

Role of Interns in Patient Care

Teamwork.—The team approach of the well-integrated house staff, although it produces some of the duplication and repetition that has been mentioned, has many advantages over the solo approach. The alert intern or resident frequently contributes as much or even more to the patient's welfare than does the attending physician or chief of the service. The house staff, working as a team, also makes indispensable contributions to the activities which go on in the highly complicated modern operating room. Without the disciplined and practiced assistance of the team the attending surgeon would not be able to perform some of his most brilliant operative feats.

Thoroughness.—The house staff adds materially to the thoroughness with which each patient is studied and treated. By reading extensively about the problems presented by their patients and by undertaking a variety of clinical tests and laboratory procedures, they may lead the diagnostic and therapeutic efforts down new and productive paths. The patient is usually wholly unaware of the extensive study of his problem which goes on behind the scenes and which frequently involves experts whom he never sees and for whose services he never pays. This is a handsome dividend of the house staff training program.

Technical Skill.—The house officer, from the frequent repetition of his daily duties, acquires a degree of technical facility which he will probably never be able to sustain during his future life as a practitioner. His technical proficiency may be likened to that of the pianist who practices many hours each day. If I needed to have a venipuncture and had to decide whether it was to be performed by a member of the house staff or the chief of the service, I would choose the house officer every time.

Availability.—In a hospital which has a house staff, a physician is available at all hours to attend to emergencies in the hospital or in the accident department. There is always a doctor to supervise protracted forms of treatment, answer patients' questions, explain procedures, allay anxieties, and either forewarn or reassure members of the patients' family.

Stimulation.—An important effect of the house staff is that it keeps the older staff members on their toes. The interchange between the two age levels probably accomplishes more than any other factor in elevating the level of patient care. It leads to the creation of an atmosphere of alertness and up-to-dateness and to the development of an *esprit de corps* which pervades the entire institution.

Medical Science—The house staff each year transmits to the hospital community fresh attitudes and factual knowledge which they have absorbed in the scientific environment of the university The farther the hospital is removed from the university the greater will be the influence and productiveness of this liaison The scientific contributions of the house staff to patient care and the frequently beneficial effects of the research in which they participate are chapters in themselves I have chosen not to dwell on the scientific activities of the house staff but rather on their contributions to the art of medicine It is in the latter field that most criticisms arise

Comment

This concludes the enumeration of the more obvious pros and cons I believe that the balance swings heavily toward the credit side Some of the items on the debit side are accretions not inherent in the training process They could be eliminated or materially reduced by appropriate action

There is one recent accretion which is particularly troublesome the fixed duty schedule for the house staff I have hesitated to list it because I am not sure that anything can be done about it The interviewer of applicants for internships is frequently asked, "What are the hours of work and what provision is made for time off?" If his answer indicates that the time off is anything less than alternate evenings after 5 p m and alternate weekends after 12 noon on Saturday it is likely to be greeted with a frown and to have an effect on the order in which the applicant ranks his selections If anyone had been impertinent enough to ask such a question in the days when my contemporaries applied for their internships, I am sure he would have been conducted to the nearest exit without delay Of course, if he were married he either kept it a deep dark secret or he just skipped over the internship and went directly into practice Social sanctions then did not embrace marriages and the fathering of three or four children by house officers who had no visible means of support, even if the wife might be able to find a job These quaint taboos of earlier decades served at least one useful purpose They made the house officer's existence a relatively simple life of learning Since he had no family responsibilities and no alter ego, he could be held strictly accountable for the way in which his patients were managed, and he was expected to respond to their calls at all hours of the day and night

The new fixed schedule of time on duty and time off duty weakens the house officer's feeling of responsibility toward his patients and interferes with the smooth management of the details of diagnosis and treatment Patients are usually quite unaware of this, but I know a number of exasperated attending physicians who fervently pray that the house staff may someday rejoin the society of celibates Although I support this prayer I realize that my attitude runs counter to a widely approved social trend Yet I cannot but feel that when this sanction of temporally limited responsibility begins at the intern level, it will inevitably affect attitudes and values at all levels of medical practice Fewer persons will want to enter solo practice in rural areas where there are no alter egos, and I would anticipate a crescendo of complaints about doctors who refuse to take night calls or any sort of calls on their days off Even worse than this would be a mass movement of young doctors toward careers which offer a 40-hour week I hope I am unduly apprehensive about this unpremeditated effect of the house staff training program

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The preceding addresses—starting on page 1289—represent the first day of the congress Second day addresses—part 2 of the symposium—will appear in the next issue of THE JOURNAL

BARTHOLOMEW COLUMBUS—When Bartholomew Columbus said Sir Hans, was sent to England by his brother Christopher, in 1488, to persuade Henry the Seventh to fit him out for this expedition, a sea chart of the parts of the world then known was produced, and a proposal made to the King, but after much delay and many untoward circumstances, both the map and the proposal were disregarded, and the money than had at first been set apart for the purpose, and thought sufficient for the discovery of the New World, was ultimately expended in the purchase of a suit of fine tapestry hangings, brought from Antwerp, and afterwards used for the decoration of Hampton Court—The Gold-Headed Cane, London, J Murray, 1828

JAMA, July 23, 1960

OVERT BEHAVIOR PATTERN IN CORONARY DISEASE

DETECTION OF OVERT BEHAVIOR PATTERN A IN PATIENTS WITH CORONARY DISEASE BY A NEW PSYCHOPHYSIOLOGICAL PROCEDURE

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A psychophysiological test was developed to detect a specific behavior pattern previously found[1] to be associated with a high incidence of clinical coronary artery disease This test consisted of the polygraph recording of various physiological reactions of subjects listening to a specially designed tape recording of two monologues The test appeared to differentiate the patient with clinical coronary artery disease from the normal subject It is suggested that tests of this sort, designed for mass application, would help to identify persons with the type of personality that predisposes to high serum cholesterol levels, faster clotting times, arcus senilis, and coronary heart disease

We have previously found[1] that groups of either men or women who exhibit a particular type of personality (which we have designated overt behavior pattern A), characterized by excessive competitive drive, a persistent desire for recognition and advancement, a persistent involvement in multiple functions subject to "deadlines," and a habitual propensity to accelerate their pace of living and working, also exhibit much higher serum cholesterol levels, faster blood clotting times, three to five times as much arcus senilis, and about seven times as much clinical coronary heart disease as control groups selected because of their apparent exhibition of a converse personality (overt behavior pattern B) The possible importance of the behavior pattern itself in the pathogenesis of these various biochemical, physiological, and clinical abnormalities was emphasized to us when the dietary drinking, smoking, exercise, and other living habits of these groups were found to be essentialy alike

These results were not particularly surprising to us, primarily because we previously had observed that behavior pattern A was almost invariably present in relatively young patients (i e, under the age of 60 years) already suffering from clinical coronary heart disease Indeed, it was this habitual finding in such patients that prompted our studies[1] to determine whether the behavior pattern was induced by the heart disease or whether the pattern itself bore an important causal relationship to the disease

In view of these findings, the detection and recognition of behavior pattern A in individual or groups of persons might be expected to have considerable prognostic as well as diagnostic value There are, however, many difficulties involved in scanning large groups of subjects for the presence of a particular behavior pattern, whether assessed by lay or by medical observers For example, the behavior pattern may consciously or unconsciously be camouflaged by the subject, or it may, in the observer's haste or superficial inspection, either be confused with various neuroses or, as is frequently the case, be entirely overlooked The last is particularly possible when the observer is not conscious of, or trained in, assessment of this particular type of pattern Then too, purely clinical assessment by one observer, defying quantitation and adequate indexes of expression, may be neither understood nor accepted by others Finally, the exclusive employment of trained physicians or other personnel for detection and assessment of this behavior pattern makes routine surveys of large groups of subjects a practical impossibility

Confronted with these difficulties, we have considered possible methods by which behavior pattern A might be both detected and assessed by even the untrained observer and without subjective bias The following report describes the use of one such method, a psychophysiological test which appears to us, from these studies, to be suitable for and applicable to detection of behavior pattern A when it is present in patients already exhibiting clinical coronary heart disease

Materials and Methods

Selection of Subjects—Three groups of subjects were chosen for the test (table 1) The first group consisted of the last 20 patients successively encountered in our private practice who met the following criteria (1) electrocardiographic evidence of coronary artery disease or history of angina pectoris or myocardial infarction, (2) no clinical or roentgenographic evidence of pulmonary or other types of cardiac disease, (3) no evidence of cardiac decompensation, and (4) aged under 60 years These

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20 patients (15 men and 5 women) therefore represent a group who were unselected except for their status as private patients and the necessity of exhibiting the above criteria

Of these 20 patients 19 clearly exhibited the characteristics of overt behavior pattern A[1] All of them admitted that they chronically harbored a marked sense of competitive drive and, most particularly, a severe sense of time urgency In addition, and most important of all, they were observed to exhibit the various motor phenomena and mannerisms we have come to recognize as part and parcel of this pattern These were (1) rapid, frequently forced, and audible intake of breath, (2) explosive intonation or emphasis of certain individual words in sentences, (3) tense facial and body musculature, (4) frequent fist clenching accompanying ordinary conversation, and (5) consistent tendency to hasten the pace of ordinary conversation by attempting either to finish the sentences of the interviewer or to hasten the latter's rate of speaking by uttering rapidly such phrases as "Yes, yes" or "I see, I see" even before the interviewer had finished his sentences

TABLE 1—*General Relevant Characteristics of Three Groups of Subjects in Study Measuring Behavior Pattern of Patients with Coronary Artery Disease*

		Incidence %						
No of Subjects*	Average Age, Yr †	Arcus Senilis	Abnormal ECG	Angina Pectoris	Old Infarct	Behavior Pattern A	Behavior Pattern B	Functional Cardiovascular Disease (FCVD)
Patients with Clinical Coronary Heart Disease								
20(5)	47(33-60)	60	85	50	50	95	5	0
Normal Subjects								
15(2)	47(34-59)	7	0	0	0	0	100	0
Patients with FCVD								
7(1)	41(21-54)	0	0	0	0	0	0	100

* Figures in parentheses indicate number of women included
† Figures in parentheses indicate range

The second group of 15 subjects (13 men and 2 women), also under the age of 60 years, were not patients selected successively as described above but normal persons who were asked to serve as controls Such subjects gave no history or clinical evidence of any type of cardiopulmonary disorder had normal electrocardiogram, and had both parents alive or surviving 65 years or more without obvious cardiac disease In addition, all subjects selected were considered by us to exhibit overt behavior pattern B, the pattern found in our earlier studies[1] to be most often free from association with clinical coronary artery disease

These subjects exhibiting behavior pattern B of course presented the converse of the characteristics observed in the coronary patients of the first group Thus, in general their positions demanded neither competitive activity nor preoccupation with deadlines None admitted having either competitive zeal or a chronic sense of time urgency None exhibited any of the motor phenomena or mannerisms described above

The third group consisted of seven neurotic subjects (6 men and 1 woman) who exhibited characteristic signs and symptoms of functional cardiovascular disease (FCVD),[2] including excessive hyperventilation, giddiness, tremor, periods of prolonged upper left thoracic distress, and excessive axillary and palmar sudation, but were free of any evidence of clinical coronary or other cardiopulmonary disease

Description of Test—In our earlier study,[1] we emphasized the habitual propensity of persons exhibiting behavior pattern A to exhibit such motor phenomena as alterations in their usual respiratory actions, hand or jaw clenching, teeth "grinding," forceful hand or fist gesturing, and excessively frequent extraneous body movements Such motor phenomena were particularly apparent to us when such persons were obliged, against their will, to slow their usual rapid pace of performing vocational functions, or when they were required to engage in an activity that they personally considered to be nonproductive or useless

Guided by these latter observations, we thought it advisable to study some of the motor phenomena of such subjects that could be graphically recorded when they were required to listen to a special monologue purposefully designed to present them with certain irritating or provocative stimuli Therefore, a slightly modified Reid-type polygraph, like that generally used in "lie detection tests," was used to record the respiratory and body movements as well as any possible hand clenching occurring in the subjects as they were directed to listen to the specially designed tape recording To obtain tracings of the respiratory excursions of both the upper and lower portions of the chest, one pneumographic recording device was placed at the level of the second and third intercostal spaces and a second at the level of the seventh and eighth intercostal spaces Any significant body movement was transmitted to the recording machine by the special Reid-type chair Any hand clenching was detected by a soft rubber bulb (partially filled with enough cotton to require a moderate hand-clenching pressure to effect displacement of the remaining air in the bulb) held in the subject's hand and connected to the recording apparatus by the channel originally designed for blood pressure recording

The tape recording consisted of two monologues, one spoken by a man, the other by a woman The male monologue, serving as a control and requiring 942 seconds for its complete audition, consisted of a discussion of the various factors generally considered essential for vocational success It was delivered evenly, relatively rapidly, and forcefully by a strong masculine voice It was of acknowledged interest to most of the subjects The presentation of this male monologue was, however, episodically interrupted 12 times by the irregular intrusion of the second monologue, whose total audition required

748 seconds This second monologue, designed as the experimental challenge monologue, deliberately and repetitively dealt with a trivial, nonsensical subject It was delivered extraordinarily slowly and very hesitantly by a soft but pleasant feminine voice The repetitive nature of the latter discussion quickly permitted the listener to foretell the end of each sentence a few seconds before it was actually spoken Unlike the male monologue, this second, female monologue frequently evoked some degree of irritation, impatience, or both in the normal and almost invariably in the coronary patients It did not appear, however, to be particularly distasteful or irritating to the patient with functional cardiovascular disease (FCVD)

The subject to be tested, after being connected to the polygraph by the channels described, was initially allowed to sit quietly without exposure to stimuli of any kind for a basal control observation period of several minutes during which the respiratory excursions and any hand clenchings and body movements were recorded Then the recorded monologues were turned on During both this basal period and the audition of the two monologues, only a trained technician remained in the room with the subject to note on the moving polygram the exact time of onset of each type of monologue as the two intermittently and irregularly interrupted each other Most subjects also were observed (without their cognizance) directly by one of us (M F) during the audition A graphic recording thus was obtained of all respiratory and body movements and of any significant amount of hand pressure on the bulb by each subject as he listened for 1,690 seconds to the two monologues

At the completion of the test, each frame of the polygram corresponding to each segment of monologue was first studied with regard to its two respiratory curves (i e, those of the lower and upper chest respectively) to determine the ratio of the length of excursion of the upper chest respiratory wave to that of the lower chest Second, the slope of the inspiratory limb of the upper chest wave was calculated and expressed as the degrees of deviation made by the inspiratory limb from a vertical axis intersecting the point at which the inspiratory limb began Third, the rate of respiration was determined Fourth, a search was made for any significant deviation, distortion, or deformity in either the contour or the size of each recorded respiratory wave Each frame finally was inspected for the presence of any recorded body movements and hand clenchings

The total number of respiratory deformities, body movements, and hand clenchings occurring in the total 13 male monologue frames was calculated, and similarly for the total 13 female monologue intervals Then the total number of respiratory deformities and body movements occurring during each total monologue was divided by the duration in seconds of each monologue, the obtained value indicating the temporal frequency of occurrence of either a respiratory deformity or body movement Finally, a M/F ratio of such occurrences in the male and female monologues, respectively, was obtained by dividing the average respective frequencies Thus, for example, if a subject was found to exhibit either a respiratory deformity or a body movement every eight seconds during the audition of the male monologue and every four seconds during the audition of the female monologue, the M/F ratio was 8 4 or 2 0, indicating that twice as many reactions had occurred during the total female monologue

Results

General Observations —The relevant clinical findings of the three groups of subjects are given in table 1 It will be observed that the occurrence of arcus senilis in patients with clinical coronary heart disease was more than eight times as frequent as in the normal subjects

Direct observation of the three groups of subjects while they were listening to the monologues frequently, but not invariably, allowed ready discrimination of the type of subject being studied Thus, most normal subjects evinced few or no outward signs of irritation, restlessness, tension, or anger during their audition Similarly there were few grossly visible changes in body position, a minimum of fidgeting and facial changes, and only an occasional change in respiratory dynamics

In sharp contrast, 13 of the 20 patients with coronary heart disease were observed directly by the viewer to fidget or even grossly change body position frequently, to alternately contract and relax their jaw muscles, to grimace with obvious irritation, exasperation, or hostility, and frequently to clench both hands into tight fists Such reactions moreover, appeared far more frequently during the portions of the slow female monologue On the other hand, mere inspection of the remaining seven patients in this group would not have revealed their less obvious body movements, hand clenchings, and respiratory deformities that the polygraph managed to record

The reactions of the patients with functional cardiovascular disease (FCVD) were observed to be rather typical, most obvious being their frequent indulgence in deep sighing respirations These however, occurred as often during audition of the male as of the female monologue of the recording While they also variously exhibited restlessness and body movement during the audition, there was no facial grimacing or obvious hand clenching or "teeth grinding"

Respiratory Findings —One of the first striking differences observed in the respiratory curves of most male and female patients with coronary heart disease was the significantly more vertical ascent of the inspiratory limbs of their total respiratory waves (fig 1), giving an average slope of 0 9 degrees from a vertical axis intersecting the beginning of the wave This more vertical ascent appeared to be almost a fixed phenomenon, being observed both during the basal control period and throughout the audition of either monologue The average inspiratory phase of both the male and female normal subjects and of those with FCVD was far less abrupt, averaging 1 9 degrees from the vertical in both groups of subjects

The second respiratory characteristic of most male and female patients with coronary heart disease was their constant inclination to exhibit a far greater excursion of the upper than the lower part of their chests in breathing (fig 1) This particular phenomenon again was observed as a fixed sign from the beginning of the basal control period to the end of both monologues While this pattern was seen infrequently in the male or female normal subject, it was as commonly observed in the patients with FCVD as in the patients with coronary disease Thus, whereas its occurrence served to differentiate the patients with coronary disease from the normal subjects, it failed to do so in regard to the patients with FCVD

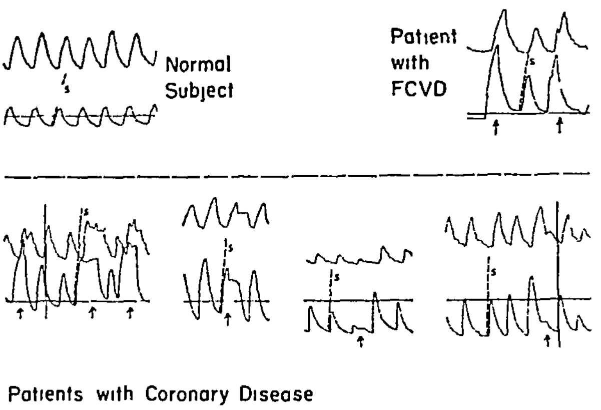

Fig 1 —Normal and abnormal respiratory patterns observed in three groups of subjects (patients with clinical coronary heart disease, normal subjects, and patients with functional cardiovascular disease [FCVD]) Upper curves represent excursions of lower portion of chest and lower curves, excursions of upper portion of chest Note slope (S) of ascending limb of respiratory excursions of normal subject and almost vertical direction of similar limb of patients with coronary artery disease Tendency of respiratory excursion of upper part of chest in coronary patient to exceed that of lower part is well illustrated in these four patients Note irregular respiratory excursions of patient with FCVD with notching of ascending limb, whereas in patient with coronary artery disease, abnormality is confined to 'plateau formations' occurring on descending limbs of respiratory curves

Besides these two described characteristics, patients with coronary heart disease also exhibited frequent deformities (fig 1 and 2) in their respiratory waves Such deformities, although they began to appear even during the initial basal control period, occurred far more often during the audition of the female monologue (once every 29 seconds of listening time) than during the male monologue (once every 54 seconds of listening time) During the total audition of both monologues, a deformity occurred once every 38 seconds The type of deformity observed in these patients was almost always caused by a hesitation on their part in expiring breath Thus, either at the apex or along the expiratory limb of the respiratory wave, a "plateau" or notch interrupting the usually observed smoothly descending line was observed (fig 1 and 2)

Normal subjects also occasionally exhibited similar respiratory deformities, but these were rarely observed during the basal control period Moreover, respiratory deformities occurred in them far less frequently during the audition of the monologues Thus, a respiratory deformity occurred an average of once every 137 seconds during the male monologue and once every 106 seconds during the female monologue During the total audition of both monologues, a deformity occurred an average of once every 107 seconds

The patients with FCVD exhibited respiratory deformities almost as frequently during the basal period and during the total audition of both monologues (once every 58 seconds) as did the patients with coronary disease However, their respiratory recordings were easily differentiated First, it was observed that the patients with FCVD uniformly exhibited respiratory distortions more frequently during audition of the male monologue (once every 48 seconds) than during the female monologue (once every 95 seconds), in contrast to the reverse pattern exhibited by the patients with coronary disease Second, the respiratory deformity usually observed in patients with FCVD was strikingly different from that observed either in the normal subjects or in the patients with coronary disease It

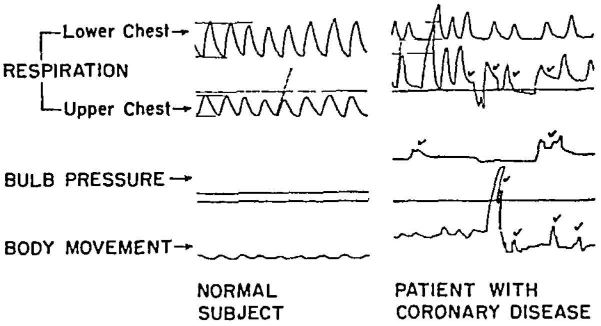

Fig 2 —Respiratory, bulb-compressing, and body movement changes in patient with coronary disease during his audition of portion of female monologue Note greater excursion of upper part of chest, more vertical ascent (S) of inspiratory limb, and plateau formations on four successive expiratory limbs of the patient compared to respiratory dynamics of normal subject auditioning same dialogue Three applications of bulb pressure and four body movements of patient also are clearly visible

usually consisted of a gross exaggeration of the total respiratory wave, with frequent notching of the inspiratory limb (fig 1) No consistent or significant change in respiratory rate was observed in the subjects of the three groups during the entire audition

Body Movements—The patients with coronary disease exhibited more body movements during the total audition (once every 307 seconds) than did the normal subjects (once every 934 seconds) Indeed although 5 of 15 normal subjects listened to the entire audition without a single body movement, only 2 of the 20 patients with coronary disease were able to do likewise The patients with FCVD changed position even more often (once every 222 seconds) than the patient with coronary disease

Hand Clenching—Perhaps none of the various recorded phenomena so clearly differentiated the patient with coronary heart disease from the other subjects as did the frequency of hand clenching Thus 14 of the 20 patients with coronary disease clenched their fists at least once during the audition of the monologues It was found that the hand bulb was squeezed by the total group an average of once every 314 seconds during the male and once every 125 seconds during the female monologue but this was never observed during the basal control period In striking contrast, no hand clenching was observed at any time in the subjects of the other two groups

Probable Significance of Results Obtained from the Test—Differentiation of a group of patients with clinical coronary heart disease from both a group of normal subjects and one composed of patients with functional cardiovascular disease (FCVD) appeared to be accomplished by the psychophysiological test used Thus five phenomena, namely, a consistently more rapid ascent of the inspiratory limb of the respiratory wave, a greater expansion of the upper as compared to the lower half of the chest, a threefold greater incidence of respiratory deformities, a twofold greater incidence of body movements, and the frequent occurrence of hand clenching, clearly differentiated the group of patients with coronary heart disease from the normal subjects

Differentiation of the patients with coronary disease from those with FCVD also was easily accomplished Again the more rapid ascent of the inspiratory limb of the respiratory wave and the hand clenching so frequently found in the patient with coronary disease was found rarely or not at all in the patient with FCVD In addition, although both groups frequently exhibited respiratory deformities, those occurring in the group of patients with FCVD were found to differ markedly in quality from those observed in patients with coronary heart disease Moreover, both these respiratory deformities and also body movements occurred far more often during the male than during the female monologue, the exact converse of the pattern of their occurrence observed in the patients with coronary disease

Possible Use of the Psychophysiological Test for Mass Predictive Studies Concerning the Occurrence of Clinical Coronary Artery Disease

The above results strongly suggest to us that patients under the age of 60 years, suffering from clinical coronary heart disease, as a group could be differentiated from groups of normal subjects and of patients with functional cardiovascular disease (FCVD) by the character of their various motor responses during the audition of the specially designed monologues The nature of the response indicated that it was not due directly to the presence of clinical coronary heart disease in these patients but to their psychological response to the monologues

It is possible, however, that the presence of organic heart disease in these patients induced the behavior pattern they exhibited and also the nature of their responses to the audition of the monologues If this is so, the test as now constructed, while capable of diagnosis, may not be useful in any study concerned with the future incidence of clinical coronary artery disease in any person still ostensibly free of the disorder

It seems to us far more likely, however, that the behavior pattern preceded the onset of the clinical disease in the cardiac patients studied herein We believe this to be true, because the same subjective and objective phenomena characterizing behavior pattern A as previously observed[1] in subjects apparently free of clinical coronary heart disease were essentially identical to those found in the patients reported here Second, if the presence of heart disease induced the psychological responses, one might expect the latter to be similar to those observed in the patients with FCVD Third, when the presence of this behavior pattern was used as an index for the classification of a large group of subjects taken from the community, such persons exhibited[1a] seven times as much heart disease as subjects having a converse pattern (B) Finally, it is difficult enough to conceive of or explain how a psychological cast or pattern can induce a pathogenetic process ending in a diseased artery, but to believe that the reverse may occur, that is, that a diseased artery is capable of inducing such traits as competitive zeal, severe sense of time urgency, and others as found in these cardiac patients, seems fantastic, particularly when many of these cardiac patients insist that they possessed such psychological traits since high-school days

It therefore seems most reasonable to us to believe that the results in cardiac patients obtained from the test we used were due to the presence of behavior pattern A and that the latter had preceded the heart disease Indeed, we initially constructed the test as a possible means of detecting this particular pattern

If, then, the test can be assumed to be capable of detecting the presence of behavior pattern A in a group of patients already suffering from clinical coronary heart disease, it is our belief that it may also be capable of similar detection of the pattern when it is present in a single subject who is still ostensibly free of disease We believe this is possible for several reasons First, the quality and intensity of behavior pattern A as previously observed[1] in subjects still ostensibly free of clinical coronary heart disease appeared to be identical to that found in the patients tested Second, our results allow the construction of criteria for the detection and assessment of this particular behavior pattern when it occurs in the single subject Therefore, in table 2, four phenomena are listed that were seen frequently in the group of patients with clinical coronary disease but less frequently or not at all in the other two groups Thus hand clenching, as well as an inspiratory slope of less than one degree, was observed frequently in the patients with coronary disease but never in subjects of the other two groups Again, most patients with coronary disease exhibited either a respiratory deformity or body movement more frequently than once every 40 seconds of listening time, but none of the normal subjects exhibited such frequency Such increased frequency of either respiratory deformity or body movement also was observed in the patients with functional cardiovascular disease (FCVD), but in these latter patients, it was during the male rather than during the female monologue that the greater number of such disturbances occurred Thus the M/F ratio (table 2) of such disturbances was less than one in these patients and invariably greater than one in patients with coronary artery disease

TABLE 2 —*Incidence of Four Particular Motor Phenomena in Three Groups of Subjects*

	Groups of Subjects		
	Coronary Heart Disease	Normal	Functional Cardiovascular Disease (FCVD)
No of subjects	20	15	7
% incidence of subjects exhibiting			
A Hand clenching	75	0	0
B Inspiratory slope <1 degree	55	0	0
C Respiratory deformity or body movement frequency >once/40 sec	90	0	71
D M/F ratio >1 0	100	66	0
% incidence of subjects exhibiting combinations of A B C & D			
1 or more	100	66	71
2 or more	95	0	0
3 or more	80	0	0
All 4	45	0	0

* M/F ratio = (frequency of combined respiratory deformities + body movements during male monologue [sec]) ÷ (frequency of combined respiratory deformities + body movements during female monologue [sec])

It can be seen by inspection of table 2 that whereas most subjects in all groups exhibited one of these four listed phenomena, none of the normal subjects or patients with FCVD exhibited two of the phenomena However, 95% of all the patients with coronary disease exhibited two or more of these phenomena, 80%, three or more of the phenomena, and 45%, all four phenomena

Hence it appears to us that any person subjected to this test, who exhibits two or more of these criteria during the audition of the challenge recording, might be considered as probably possessing the characteristics of overt behavior pattern A The possession of this particular behavior pattern in a subject does not, however, indicate that he has, or will necessarily contract, coronary heart disease It only implies, if the results of our other studies[1] have been correctly interpreted, that his chances of future susceptibility to clinical coronary heart disease will be markedly enhanced Studies designated to test this hypothesis are now being initiated

Summary

A tape recording was made of two monologues frequently interrupting each other One of these monologues, the challenge monologue, consisted of inane subject matter that was delivered repetitiously in a slow, hesitant manner Twenty patients with clinical coronary heart disease, 15 normal subjects, and 7 patients with functional cardiovascular (FCVD) disease were asked to listen to this tape recording

The respiratory excursions, body movements, and possible indulgence in hand clenching of these patients were graphically recorded as they listened to the two monologues It was found that the group of patients with coronary heart disease exhibited respiratory and hand clenching phenomena that clearly differentiated them from the other two groups This particular test may lend itself to mass predictive studies

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Donna Cary, B S , and George W Harman rendered technical assistance in the preparation of this study

This study was supported by grants from the Alameda County Heart Association, Contra Costa Heart Association and Life Insurance Medical Research Fund

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We believe that this postural change in splitting of the second heart sound separates persons in whom this is a normal variant from those in whom splitting is a sign of cardiac disease. We recommend, therefore, that clinical analysis of the second heart sound be performed with the patient in the erect position.

Summary

Splitting of the second heart sound is called physiologic if it disappears on expiration. This change can be appreciated by auscultation. A persistently split second heart sound with the patient in the supine position may be normal or may indicate cardiac disease. In some cases seemingly pathological splitting of the second heart sound disappears when the patient changes from the supine to the upright position. The interpretation of a persistently split second heart sound should be carried out with the patient sitting or standing.

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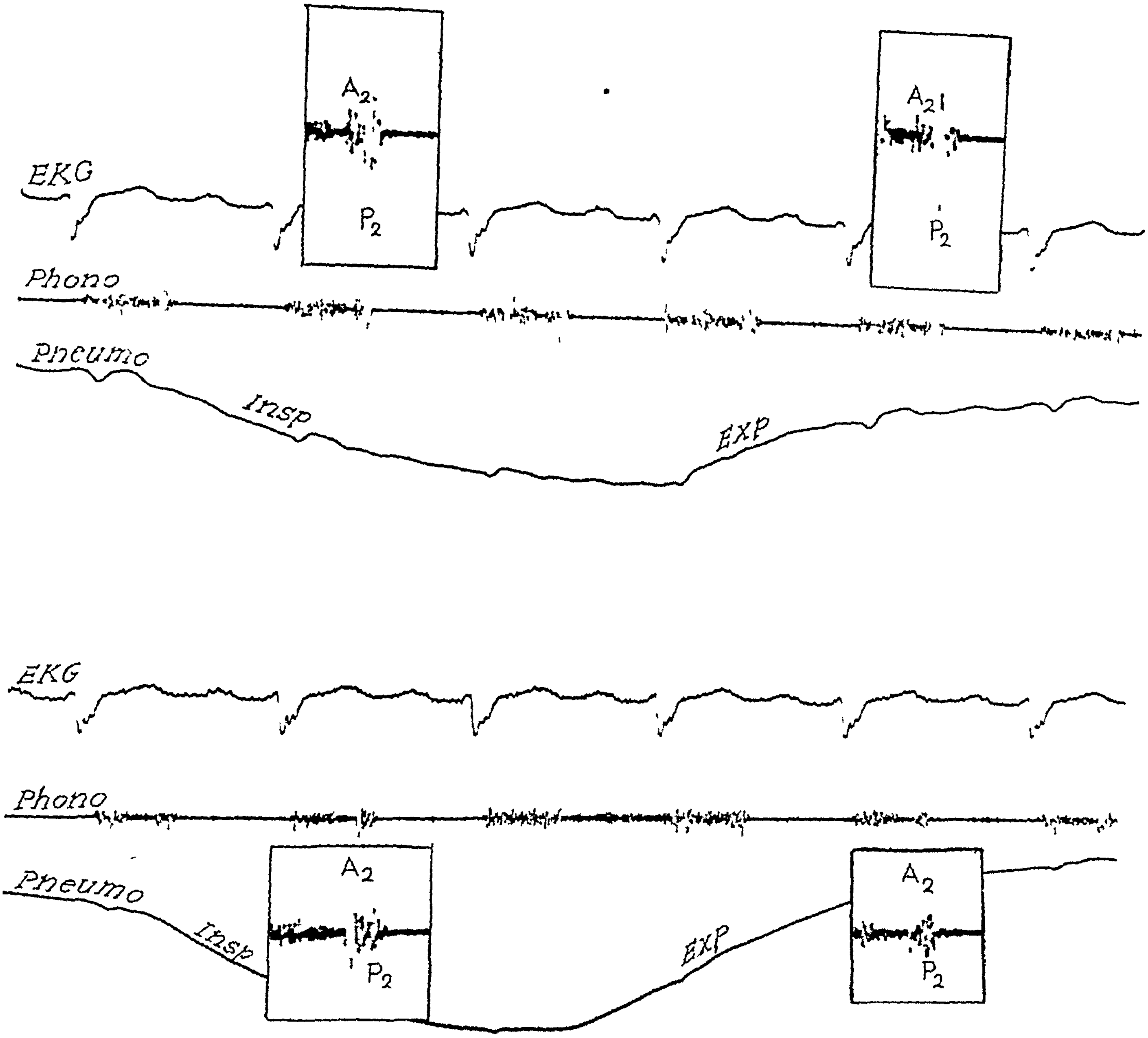

Fig. 2.—Electrocardiographic and phonocardiographic record of 41 year old man with large ostium primum defect proved at operation. There is fixed persistent splitting of S_2 with patient both supine (*above*) and sitting (*below*). P_2 follows A_2 by 0.04 to 0.05 seconds.

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ELECTROENCEPHALOGRAM AND MYOPATHY

RELATION BETWEEN MUSCULAR DYSTROPHY AND RELATED DISEASES

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and
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Electroencephalographic findings in 101 patients with muscular dystrophy and related myopathies are reported Abnormal electroencephalograms were found in a total of 39 patients 45% of 62 patients with pseudohypertrophic muscular dystrophy, 18% of 22 with amyotonia congenita, 37% of 8 with facioscapulohumeral dystrophy, and 45% of 9 with other myopathies and related syndromes The most common abnormalities in the electroencephalogram were 14 and 6 per second positive spikes, seen especially in patients with pseudohypertrophic muscular dystrophy Other abnormalities were spike seizure discharges, fast or slow frequency, asynchronous sleep patterns, and amplitude asymmetries The electroencephalographic abnormalities increased with advancing age but were not related to severity of the seizures It is suggested that the high incidence of abnormal electroencephalograms in patients with muscular dystrophy may be due to basic maturational neurophysiological involvement, an integral part of muscular dystrophy

In most studies on the myopathies, attention has been focused on muscle tissue per se It is only recently that the central nervous system, the blood serum, the cardiovascular system, and other areas have come under scrutiny We have long been aware that many patients with muscular dystrophy exhibited abnormalities in the electroencephalogram To our knowledge, there was no mention in the literature of this observation until the recent reports by Winfield, Britt, and Raskind [1] and by Wayne and Brown-Mayers,[1A] who found abnormal electroencephalograms in patients with pseudohypertrophic muscular dystrophy (PHMD) The present report describes the electroencephalographic findings in 101 patients with muscular dystrophy and related myopathies

Population and Methods

The patients in this study were all evaluated by the same clinician, one of us (M A P), in private practice, at the children's neurology clinic of Cook County Hospital, and at the Illinois Children's Hospital School For purposes of this study, they were grouped into four diagnostic categories (table 1)

Pseudohypertrophic Muscular Dystrophy—Pseudohypertrophic muscular dystrophy is the most common form of muscular dystrophy seen in children There were 62 children with this diagnosis, most of them over 2 years of age

Amyotonia Congenita—The second largest category, with 22 patients, most of them seen during infancy, was that of amyotonia congenita This group included both the static (Oppenheim) and progressive (Werdnig-Hoffman) forms

Facioscapulohumeral Dystrophy—There were eight patients with facioscapulohumeral dystrophy, most of them over 5 years of age This form of muscular dystrophy is more commonly seen in older children and young adults For this study, patients with or without facial involvement were grouped together

Other Myopathies or Related Syndromes—There were nine patients with other myopathies or related syndromes, one with peroneal atrophy, three with atypical, rapidly progressive muscular dystrophy but without pseudohypertrophy (femoral type), and five with unclassified slowly progressive or static types of myopathies The severity of involvement was clinically graded into three stages (*a*) mild, with waddling gait, lordosis, slight to moderate difficulty in stair climbing, but ability to arise from the floor, (*b*) moderate, with inability to arise from the floor but ability to walk short distances unaided, and (*c*) severe, with wheelchair or bedridden existence and varying degrees of help needed for activities of daily living

All electroencephalographic recordings were made in the laboratory of two of us (F A G and E L G), with an eight-channel electroencephalograph Monopolar leads were used, with electrodes over both frontal, parietal, occipital, and temporal areas, with an electrode on one ear lobe or both used as a reference point Tracings were made with the patients both awake and asleep In some patients who were unable to fall asleep spontaneously, sedation with either chloral hydrate or pentobarbital given orally or rectally was used If sleep was not obtained even with sedation, the electroencephalogram was excluded from this study

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Repeated electroencephalograms were done on many patients, and seven of these are included in this report as separate records because they differed from the first record, by normalization or abnormalization

TABLE 1 —*Electroencephalographic Data by Diagnostic Category*

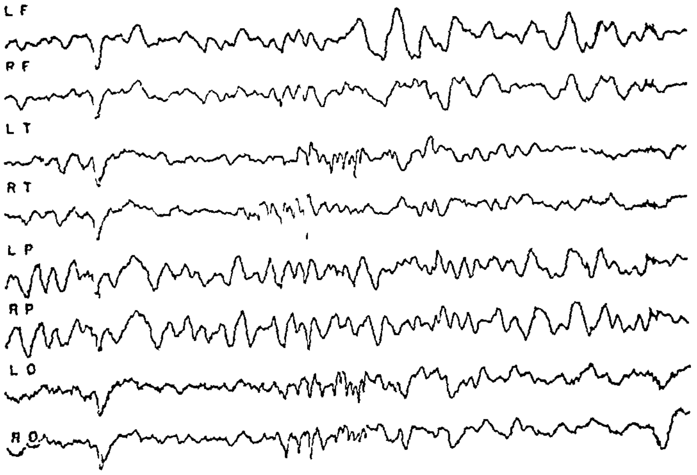
Diagnosis*	Patients, No	Abnormal EEG		Type of Abnormality	
		No	%	14 and 6	Other
PHMD	62	28	45	22	6
AC	22	4	18	3	1
FSH	8	3	37	2	1
Other	9	4	45	0	4
Total	101	39	39	27	12

* *PHMD* = pseudohypertrophic muscular dystrophy AC = amyotonia congenita and FSH = facioscapulohumeral muscular dystrophy

Results

From table 1 it can be seen that of the 101 patients with muscular dystrophy, 39% had abnormal electroencephalograms When the various diagnostic categories are inspected, it is noted that abnormal records were more common in patients with pseudohypertrophic muscular dystrophy (45%) than in those with amyotonia congenita (18%) The incidence of abnormal electroencephalograms in patients with the facioscapulohumeral type (37%) and in those with "other myopathies" (45%) was also rather high

Type of Abnormality—In patients with epilepsy or with cerebral palsy, the most common abnormalities seen in the electroencephalogram are seizure spikes of various types It was therefore of interest to note that in this group of patients with myopathies, 14-and-6-per-second positive spikes was the most frequent abnormality, occurring in 27 of the 39 (69%) abnormal records (see figure) This high incidence of 14-and-6-per-second positive spikes was most conspicuous in the patients with pseudohypertrophic muscular dystrophy, of whom 22 of 28 (80%) with abnormal electroencephalograms had this abnormality Although the number of patients with abnormal electroencephalograms in each of the other categories may be too small for statistical significance, it is interesting to note that three of four abnormal electroencephalograms in the patients with amyotonia congenita and two of three in those with facioscapulohumeral dystrophy had 14-and-6-per-second positive spikes None of the four patients with abnormal electroencephalograms in the "other" group had 14-and-6-per-second positive spikes Of the 12 electroencephalographic abnormalities other than 14-and-6-per-second positive spikes, 4 were spike seizure discharges, 3 were fast and 1 was slow frequency, 2 were asynchronous sleep patterns, and 2 were amplitude asymmetries



Tracing of 14-and-6-per-second positive spikes in patient with pseudohypertrophic muscular dystrophy

Relationship to Age—Table 2 depicts the relationship of age to abnormalities in the electroencephalogram In this table there were 108 electroencephalograms done on 101 patients, since 7 were included which changed with age It is obvious that with advancing age there is an increase in the number of abnormal electroencephalograms In the 15 children aged under 2 years, no abnormalities were noted In the 2-to-6-year age group, 8 of the 32 (25%) were abnormal In the 7-to-11-year age group, 21 of the 45 (47%) electroencephalograms were abnormal, in the 12-to-16-year group, 9 of 14 (64%) were abnormal, and one of the two electroencephalograms in the group aged over 17 years was abnormal

TABLE 2 —*Relations Between Electroencephalogram and Age*

Age Yr	Patients, No	Abnormal EEG		14 and 6/Sec Spike
		No	%	
<2	15	0	0	0
2 6	32	8	25	3
7 11	45	21	47	15
12 16	14	9	64	8
>17	2	1	50	1
Total*	108	39	36	27

**108 EEG s on 101 patients include 7 repeat tests which changed with age*

It is noteworthy that the frequency of 14-and-6-per-second positive spikes as the dominating abnormality also increased with age In the 2-to-6-year age group, three of the eight abnormal records (37%) had 14-and-6-per-second positive spikes, in the 7-to-11-year age group, 15 of the 21 (71%) abnormal electroencephalograms, in the 12-to-16-year group, eight of nine (89%) abnormal electroencephalograms, and in the group aged over 17 years the single abnormal electroencephalogram had 14-and-6-per-second positive spikes The increase of abnormalities in the electroencephalogram, particularly of the 14-and-6-per-second positive spikes, with advancing age was characteristic of patients with all types of muscular dystrophy

Relationship to Severity of Condition—Table 3 shows the relationship between the severity of muscular dystrophy and the incidence of abnormal electroencephalograms for the whole series and for patients with pseudohypertrophic muscular dystrophy alone For the whole series, 29% of the mildly involved patients, 44% of the moderately involved, and 40% of the severely involved had abnormal electroencephalograms Since our figures might be skewed by the fact that the patients with amyotonia congenita, all of whom had severe involvement, had relatively fewer abnormal electroencephalograms than the patients with other types of muscular dystrophy, the data were also tabulated for patients with pseudohypertrophic muscular dystrophy alone When the figures for this group are inspected, there is a marked increase in abnormal electroencephalograms, with severity increasing from 28% in the mildly involved to 62% in the severely involved group

Table 3—*Relations Between Electroencephalogram and Severity of Disease*

	Total Series			PHMD*		
		Abnormal EEG			Abnormal EEG	
Stage	No	No	%	No	No	%
Mild	45	13	29	32	9	28
Moderate	18	8	44	11	6	55
Severe	45	18	40	21	13	62
Total	108†	39	36	64‡	28	44

* Patients with pseudohypertrophic muscular dystrophy
† 7 repeat electroencephalograms on 101 patients
‡ 2 repeat electroencephalograms on 62 patients

Since severity often progresses with age, it is not clear from table 3 whether age or severity of involvement is responsible for the increased number of abnormal electroencephalograms A comparison was therefore made of the incidence of abnormal electroencephalograms according to severity in a single age group and according to age in a group with disease of given severity (table 4) In the group of patients with pseudohypertrophic muscular dystrophy, there was only one age group, 7 to 11 years, with enough cases for comparison The severity of the condition had no relation to the incidence of abnormal electroencephalograms or to the predominance of 14-and-6-per-second positive spikes in this age group, in all three groups the incidence of abnormal electroencephalograms varied from 45 to 56% On the other hand, in both the mildly and the severely involved groups, the only such groups with sufficient cases for comparison, there was a marked correlation between the incidence of electroencephalographic abnormalities and age In the mildly involved, the incidence of abnormal electroencephalograms rose from 16% in the 2-to-6-year age group to 50% in the 7-to-11-year group In the severely involved, it rose from 46% in the 7-to-11-year group to 80% in the 12-to-16-year group In all of these, 14-and-6-per-second positive spikes made up over 80% of all the abnormalities

Comment

The significance of the high incidence of abnormal electroencephalograms in patients with muscular dystrophy and related myopathies is not clear Generally, one might expect that in a condition characterized by the presence of a great many abnormalities in the electroencephalogram there would be an increased frequency of seizures of various types This is certainly not the case in muscular dystrophy In our experience with about 400 patients with various types of muscular dystrophy, most of them pseudohypertrophic and amyotonia congenita, we have not encountered a single patient with a clinical seizure, nor has a survey of the literature or personal communications from experienced clinicians brought to our attention the presence of seizures in patients with muscular dystrophy In fact, seizures cannot be induced in patients with pseudohypertrophic muscular dystrophy or amyotonia congenita, even by the administration of large doses of strychnine[2] In this series there were three children with pseudohypertrophic muscular dystrophy who had classic spike seizure patterns in their electroencephalograms, none of whom had had a clinical seizure

The extremely high incidence of 14-and-6-per-second positive spike seizure discharge in muscular dystrophy is also difficult to explain This type of abnormality is presumably due to a disturbed neuroelectrical status arising from the midbrain[3] and is highly correlated with the presence of vegetative seizures, behavioral episodes, and many so-called atypical seizures and emotional disturbances Unpublished data indicate that for a normal population (excluding patients with epilepsy, "possible" epilepsy, or other neurological conditions) the incidence of 14-and-6-per-second positive spikes varies from 6% in the 2-to-4-year age group to a high of 15% in the 15-to-20-year age group and then declines to 3% in the adult population Our finding of an increasing frequency of 14-and-6-per-second positive spikes, from 0% in children aged under 2 years to 25% in the 2-to-4-year age group to 47% in the 7-to-11-year age group and to 64% in the 12-to-16-year age group, represents a pronounced increase in this electroencephalographic abnor-

Table 4—*Relations Between Electroencephalogram, Age, and Severity of Disease in Patients with Pseudohypertrophic Muscular Dystrophy*

	Patients	Abnormal EEG	
7 11 Yr Age Group Involvement	No	No	%
Mild	10	5	50
Moderate	9	5	56
Severe	11	5	45
Mild involvement age yr			
2-6	19	3	16
7 11	10	5	50
Severe involvement age yr			
7 11	11	5	46
12 16	10	8	80

mality, although it conforms at least in part to the distribution in the "normal" population by its increasing frequency with age

In our material it was noted that 14-and-6-per-second positive spikes were found with greater frequency in patients with the pseudohypertrophic (45%) and facioscapulohumeral (37%) types of muscular dystrophy than in those with amyotonia congenita (18%)

There are two possible explanations for the surprisingly high incidence of electroencephalographic abnormality, especially 14-and-6-per-second positive spikes, in patients with muscular dystrophy (1) muscular dystrophy is not a disease of muscles only but is a generalized disturbance, with changes in most or all of the other organs, tissues, and metabolic systems, or (2) the high incidence of 14-and-6-per-second positive spikes may be a reflection of the disturbed emotional status of these patients, who are handicapped and whose emotional problems increase as they approach puberty

It is likely that both of these possibilities are operative to a certain extent Evidence for the first possibility is forthcoming from studies which indicate that many systems are involved in muscular dystrophy For instance, about 30% of these patients have abnormal electrocardiograms, most commonly a partial right bundle-branch block On electromyographic examination, in addition to the characteristics of degenerating muscle (i e, dystrophic, polyphasic, and fibrillatory potentials), patients with pseudohypertrophic muscular dystrophy often evince myotonic runs, indicating hyperactivity and hyperirritability of muscle Psychological testing reveals that for the group with pseudohypertrophic muscular dystrophy, the average intelligence is slightly lower than normal, not only for the patients but also for their uninvolved siblings Studies on the blood serum have shown increased contents of certain enzymes, particularly an elevation of aldolase (fructose-1-PO_4-aldolase), dehydrogenase (lactic acid dehydrogenase), and transaminase (serum glutamic oxalacetic transaminase) In light of the findings of abnormal electrocardiograms, electromyograms, and serum enzymologic studies and subnormal intelligence, one might infer that the high incidence of abnormal electroencephalograms is additional evidence that muscular dystrophy is a generalized disease with predominantly muscular manifestations

The other possibility to consider is that the increase in the incidence of 14-and-6-per-second positive spikes may be a reflection of the disturbed emotional status of these patients, due to their long, debilitating disease, which in some manner influences the process of neurophysiological maturation It has been observed that patients with other chronic debilitating diseases such as poliomyelitis, postencephalitis, or rheumatic fever may also evince a relatively high incidence of 14-and-6-per-second positive spikes, also directly related to age In each of the aforementioned examples of chronic disabling diseases, however, there might well be organic involvement of the central nervous system to account for the electroencephalographic abnormalities, since it is well known that all of them may have central nervous system complications In fact, acute infectious diseases such as measles, mumps, and pertussis, without clinical evidence of nervous system involvement and without other chronic sequelae, may result in an increased incidence of 14-and-6-per-second positive spikes, with or without emotional disturbances To our knowledge there has been no study on the incidence of 14-and-6-per-second positive spikes in the so-called normal population of the chronically disabled, without tendencies toward central nervous system involvement, e g, amputees, patients with fractures, or those forcibly confined with no physical disability

It is not likely that the emotional disturbances and frustrating experiences of the patients with muscular dystrophy would in themselves be responsible for the increased incidence of 14-and-6-per-second positive spikes, since similar changes are not characteristically seen in psychotic patients or those with functional emotional problems It would, therefore, appear that the increased incidence of 14-and-6-per-second positive spikes in patients with muscular dystrophy reflects the existence of a neurological component in muscular dystrophy

The observation in this study that the incidence of electroencephalographic abnormality is related not to the severity of the disease but rather to the age of the patient would indicate that the neurological involvement is not so much an intrinsic morbid anatomic defect as a physiological one, modulated by maturational and developmental factors The mechanism responsible for the increased incidence of 14-and-6-per-second positive spikes with age may be the same factor responsible for the emotional problems that likewise become more manifest in these patients as they get older The much lower incidence of abnormal electroencephalograms in patients with amyotonia congenita than in those with pseudohypertrophic and facioscapulohumeral muscular dystrophy indicates that amyotonia congenita may be different in nature from the true progressive myopathies A similar difference was found to exist in the electromyographic characteristics of patients with amyotonia congenita and the progressive myopathies[4] Clinically, also, there is much evidence that many patients with amyotonia congenita have prenatally acquired myelopathies rather than genetic disease of muscle

The value of the electroencephalogram in muscular dystrophy is primarily for its ancillary, didactic, and research values rather than for diagnostic help, since there is no specific electroencephalographic abnormality which has either diagnostic or prognostic value in this disease Such studies may, however, elucidate the basic nature of the malady, particularly insofar as the central nervous system is concerned

Summary

Electroencephalograms done on 101 patients with muscular dystrophy and related myopathies showed abnormalities in 39%, the most in those with pseudohypertrophic muscular dystrophy (45%) and the least in those with amyotonia congenita (18%) The most common abnormality found was the 14-and-6-per-second positive spike pattern, which accounted for 80% of all abnormalities in patients with pseudohypertrophic muscular dystrophy The incidence of abnormal electroencephalograms and of 14-and-6-per-second positive spikes increases with age but is not related to the severity of the disease It is suggested that the high incidence of abnormal electroencephalograms, especially 14-and-6 per-second positive spikes, in patients with muscular dystrophy may be due to basic maturational neurophysiological involvement, constituting an integral part of muscular dystrophy

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Dr Sophia Rimke, of the Illinois Children s Hospital School in Chicago, cooperated in making patients at that institution available to us

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PARAPLEGIA FROM TREATMENT WITH SCLEROSING AGENTS

REPORT OF A CASE

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A 53-year old woman suffering from lower back pain was given injections of some unknown substance into both sacroiliac regions to correct "relaxation of the ligaments" This was immediately followed by severe pain and temporary paralysis of her legs and bladder A brief period of improvement was succeeded by complete spastic paraplegia Laminectomy disclosed severe proliferative leptomeningitis There was no lasting improvement Complications resulting from the injection of sclerosing agents in the lower back in other reported cases bear out the conclusion that such use is inadvisable That the treatment is of any value is not at all evident

The treatment of pain in the lower part of the back with sclerosing materials can result in severe, permanent damage to the central nervous system This form of treatment is based on a supposition that some low back pain is caused by relaxed ligamentous supports that allow instability of the sacroiliac and lumbosacral joints It is further believed that the injection of the sclerosing material will produce a proliferative inflammatory reaction within the weakened ligaments, firm up’ the supporting structure of the lower part of the back, and relieve the patient’s symptoms[1] This report concerns a patient treated in this manner who developed a permanent, complete, spastic paralysis of her legs

In 1953 a 53-year-old woman began to suffer from a dull pain in the right side of the lower part of her back Later this pain spread to the left side

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From the Northwestern University School of Medicine and the Section on Neurological Surgery of the Chicago Wesley Memorial Hospital of the lower part of the back and right hip In March, 1957, she consulted a physician who injected "vegetable oil and anesthetic" into each sacroiliac region After the injection she developed severe pain which radiated from the site of injection around to the front and inner aspect of both thighs and down the medial surface of the lower extremities to the ankles The pain in the sacroiliac region persisted for three weeks, but the pain that had radiated into the lower extremities subsided by the next morning About May 12, 1957, she received two more injections into each sacroiliac area and another injection into one side of the spine, for "relaxation of the ligaments" Immediately she experienced severe pain across the lower part of her back, which radiated down both legs and a numbness over her body below the umbilicus When she tried to walk her legs would not support her, and she was unable to urinate for several hours These symptoms subsided by the next morning One week later she awakened with a severe headache which recurred daily for two weeks During this period she had a stiff neck and pain in the right shoulder About July 1, 1957, she began to drag both feet as she walked, and within three or four weeks she required a cane and had to hold on to furniture or walls Numbness returned to her lower extremities and grew more severe In August, 1957, a lumbar myelogram was performed at another hospital This and the examination of the spinal fluid gave negative findings except for a total protein content in the spinal fluid of 68 mg % By Sept 1, 1957, she was unable to walk Urinary frequency and occasional incontinence developed, finally, she could not urinate and became severely constipated

When admitted to the Chicago Wesley Memorial Hospital on Oct 1, 1957, the patient had a complete spastic paraplegia with the usual reflex changes There were analgesia below the 5th rib on the left side and the 6th on the right, complete anesthesia from the 8th thoracic through the third lumbar dermatomes on the left side, and hypesthesia in the remainder of the analgesic area Vibratory sensibility, sense of position, and the perception of numbers written on the skin were all absent bilaterally below the costal margins Roentgenographic examination revealed a small residue of radiopaque material in the spinal canal at the level of the 6th thoracic vertebra This material did not move as the patient was tipped on the fluoroscopic table

On Oct 7, 1957, when a laminectomy of the 5th, 6th, and 7th thoracic vertebrae was performed, the epidural fat was tougher than normal and quite adherent to the dura mater, which was humped backward at the level of the 6th thoracic vertebra as though a tumor were within On incision, the dura mater was closely adherent to the underlying structures throughout the area exposed by the laminectomy of these three vertebrae It was finally stripped away from the arachnoid membrane and the spinal cord There was a subarachnoid cyst at the level of the 6th thoracic vertebra, measuring about 1 by 2 5 cm It was evacuated, and a great amount of thickened arachnoidal tissue was cut away, including the walls of the cyst At the close of the procedure there was no evidence of constriction of the spinal cord, which was pulsating freely

Microscopic Examination —The material removed at operation consisted mostly of dense, collagenous fibrous tissue The part of a nerve root removed with the specimen was surrounded and bound down by a layer of fibrous connective tissue Certain areas of the thickened arachnoid had a loose reticular appearance A few chronic inflammatory cells infiltrated the denser areas of the fibrous connective tissue

Postoperative Course —For a time the patient's condition improved slightly, but soon the spastic paraplegia returned to its original intensity and ultimately grew more severe Flexor spasm developed and became annoying Intensive physiotherapy brought about no improvement She was discharged from the hospital on Dec 28, 1957, and since then there has been no improvement in her condition

Comment

A reconstruction of the pathogenesis of chemically induced adhesive arachnoiditis in man is largely based on observations of chronic arachnoiditis produced experimentally in animals Several investigators[2] tracing the course of experimentally induced arachnoiditis, have found a stereotyped pattern of intraspinal reaction to various chemical irritants An acute phase, resulting from a variable degree of superficial damage by the irritant to nervous tissue, is shown histologically both in peripheral nerves and the spinal cord Next, there occurs an acute leptomeningitis which lasts several days If cellular proliferation and fibrin deposition is extensive, the flow of cerebrospinal fluid is blocked Finally, over a period of several weeks, a dense fibrous connective tissue is produced which obliterates the subarachnoid pathways, compresses the spinal cord, and eventually causes multiple areas of myelomalacia and cavitation within the substance of the spinal cord

In this case, apparently, the unknown material injected into the patient's back was actually introduced into the spinal canal Initially it produced severe pain and marked neurological dysfunction in the lower extremities This acute irritation soon subsided, but evidence of a leptomeningitis (headache, stiff neck, and pain in the shoulder) soon appeared and lasted for two weeks In the ensuing weeks a chronic irritation persisted which provoked a severe proliferative process in the spinal leptomeninges This fibroblastic proliferation involved the spinal nerve roots and the spinal cord, gradually impaired the function of these structures, and produced a severe spastic paraplegia

Our case is not the sole example of a disastrous complication which resulted from the injection of sclerosing agents into the lower part of the back Schneider, Williams, and Liss[3] reported the case of a 50-year-old woman who was referred to them after she had been given an injection of zinc sulfate in 2 5% phenol solution The needle was inserted in the midline of the lower part of the back and directed toward the ligaments of the lumbosacral joint The patient developed immediate paraplegia and severe pains in both legs Although she continued to have impairment of bowel and bladder function, she recovered nearly complete use of the legs in several days Six months after the injection, she developed signs and symptoms of an extensive adhesive arachnoiditis and a marked hydrocephalus Attempts to relieve the hydrocephalus were unsuccessful, the patient died shortly after a suboccipital craniectomy had been performed Postmortem examination showed an inflammatory reaction involving the entire neural axis The most marked changes were in the lower part of the spinal cord Dense connective tissue fused the dura mater with the leptomeninges, compressing the spinal cord, a similar situation was found at operation in our patient Another similarity between the two patients is that each had immediate, severe and brief interruption of function of the spinal cord In both patients this acute phase was followed by a latent period of slight impairment of function of the spinal cord which lasted several weeks before the final severe and persistent symptoms developed

Latency of severe, permanent disability is also characteristic of the neurological complications resulting from the injection of other substances into the subarachnoid space for diagnosis or anesthesia, this can be a pitfall in diagnosis Kennedy and associates,[4] Williams,[5] and Payne[6] reported a number of cases of chronic arachnoiditis, apparently associated with spinal anesthesia, in which the patients presented signs and symptoms of involvement of the thoracic spinal cord several months after the spinal anesthetic had been administered Erickson[7] reported a patient who developed chronic arachnoiditis and hydrocephalus several weeks after pantopaque myelography had been performed Bucy and Spiegel[8] described a case in which the introduction of iodized oil (Lipiodol) into the spinal subarachnoid space was followed by the development of symptoms of the local involvement of the spinal cord in the middle of the thoracic region Although the pathological changes begin with the introduction of the irritant into the cerebrospinal fluid and continue inexorably to a final stage of severe adhesive arachnoiditis, the permanent neurological deficits may appear only after a latent period of several months

Intraspinal injections for whatever purpose—anesthesia, localization of intraspinal lesions, intrathecal therapy—sometimes cause serious neurological complications Intrathecal injections of streptomycin[9] and sulfonamides[10] are apt to cause severe reactions in the spinal cord, but serious neurological complications after spinal anesthesia or myelography are relatively uncommon

Treating pain in the lower part of the back with injections of sclerosing agents is inadvisable There is no clear-cut evidence that this method of therapy is of value As Schneider and his associates emphasized there are areas in the lower part of the back where a needle can accidentally and easily enter the subarachnoid space This can occur directly at the lumbosacral joint or laterally at the dural sleeve of a spinal nerve root The risk of permanent, disabling neurological deficits is too great to justify the use of sclerosing agents for treating back pain, particularly in view of the uncertain anatomic basis on which the treatment rests and the inadequate evidence that the treatment is of any value

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J A M A, July 23, 1960

SCIATIC NERVE INJURY IN INFANTS

RECOGNITION AND PREVENTION OF IMPAIRMENT RESULTING FROM INTRAGLUTEAL INJECTIONS

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Serious sciatic nerve injury can result from injections of commonly used antibiotics and other agents into the buttock, especially in young infants. Such injection injury occurs in the hands of those experienced in the care of infants and children. Twelve cases are reported; in most of these a paralytic drop foot resulting from nerve injury has been misdiagnosed as a congenital lesion or the result of unrecognized poliomyelitis. Demonstration of sensory loss and the absence of sweating over the distribution of sciatic nerve branches is the most valuable clue to the diagnosis. Surgical exploration of the buttock in the three most recent cases revealed marked scarring in and about the sciatic nerve. Recovery has been poor in this important, preventable, type of peripheral nerve injury which probably occurs more commonly than is usually supposed. The midanterior thigh is the preferred site for all intramuscular injections in infants and young children.

Anyone concerned with infants and children must be aware that injection into the buttock may cause paralysis in the lower extremity. It is not often recognized that serious sciatic nerve injury can result from intragluteal administration of therapeutic and prophylactic agents. Injection injury of the sciatic nerve is more common than supposed and may be responsible for paralytic deformities which may be misdiagnosed as congenital club feet or the sequelae of poliomyelitis. The newborn infant, and especially the small premature infant, is more likely to suffer from this complication. Any age group is vulnerable, and injury may result from a solitary injection. By abandoning the intragluteal site and choosing another area for intramuscular injections, physicians may spare their patients unnecessary handicaps.

Diagnosis

This communication concerns 12 infants in whom sciatic neuropathy occurred after intragluteal injection. The usual presenting complaint was paralytic drop foot (fig. 1 and 2). Examination revealed sensory and autonomic deficit in the foot and leg. Further history revealed that the extremity had been normal prior to one or more intramuscular injections, which had been given for a variety of reasons (table 1).

Sensory examination is time consuming but vital to the establishment of the diagnosis of peripheral nerve injury. Associated sensory deficit was best demonstrated when the infant was held quietly with his attention directed away from the examiner, or during light sleep. Perception of cutaneous pinprick or of light touch was tested starting in the area suspected of being anesthetic, and working toward areas of normal sensation. Lack of response characterized the area of sensory loss, whereas application of the pin to normal areas evoked withdrawal of the leg or vocal acknowledgement. Anhydrosis in the same area as the sensory deficit was demonstrated by use of the iodine-starch cutaneous sweating test[1] or by the cobalt-chloride sweat pattern[2] visualization (fig. 3).

Appearance of the Involved Extremity

The abnormal attitude of the foot as a result of paralysis was the most striking finding. Both talipes equinovarus and calcaneovalgus deformities were observed. In the infants most severely paralyzed the lower leg and foot were entirely flail below the knee, and the hamstring muscles in the posterior thigh were weakened. Other infants showed combinations of tibial division and peroneal division paralysis, including sensory and autonomic deficit of both divisions. The musculature of the lower leg and foot atrophied in the weeks after injury. This was obvious by gross inspection and palpation and was confirmed by measurement. The growth of the affected foot was retarded. Growth was resumed after several months, although even as long as two and one-half years after injury the involved foot had not reached the same size as the unaffected one.

The color and temperature of the affected foot differed from the normal foot for several months. In some infants the injured foot was flushed and warmer, in others it was initially pale and cooler. Sympathetic block could explain the former and irritation of sympathetic fibers could explain the latter phenomenon. The skin of the affected foot and ankle became thin, shiny, and often edematous. As in most extremities that have sustained a peripheral nerve injury, susceptibility to minor trauma

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and difficulty in healing occurred in several instances

Sciatic Nerve Exploration

The three most recent cases have been explored surgically and in each the gross neuropathology involved the sciatic nerve in the buttock Infant 1 had sustained complete sciatic nerve paralysis after 90 injections At operation she was found to have marked scarring in and about the sciatic nerve over a considerable segment, extending well into the thigh (fig 4) Infant 11 had a calcaneovalgus foot deformity, with paralysis of calf muscles, plantar flexor and inverter muscles of the foot, and sensory and sweating deficit involving the tibial division She had received 36 injections At exploration there was scarring at the sciatic notch only Infant 12, aged 2 years, had a talipes equinovarus foot deformity, paralysis of the calf muscles, and sensory deficit in the peroneal distribution noted two days after a single intragluteal injection of tetracycline Sensory and motor deficit persisted for five weeks, at which time scarring about the sciatic notch was found

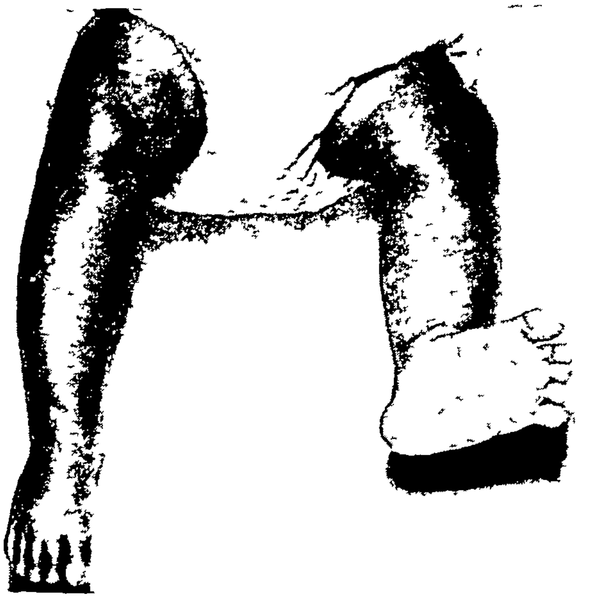

Fig 1 —Photograph of legs of patient with typical drop foot attitude, flail right leg resulting from paralysis of both divisions of sciatic nerve, three months after injections

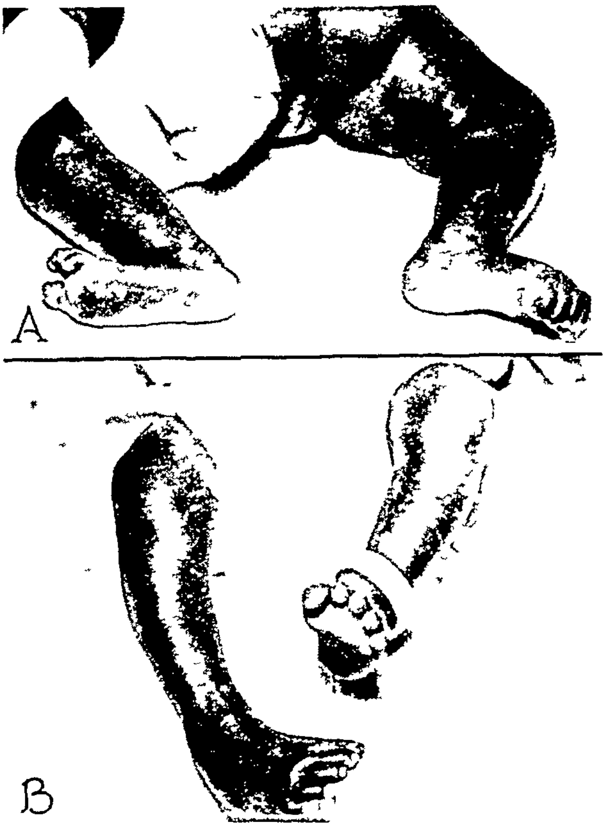

Fig 2 —Characteristic attitudes of fixed deformities resulting from *A*, damage to tibial division of left sciatic nerve and *B*, damage to peroneal division of right sciatic nerve

TABLE 1 —*Occurrence and Course of Sciatic Nerve Injury Due to Intramuscular Injection in Buttock in Twelve Infants*

Case No	Diagnosis	Premature	Age at Time of Injection	Age Recovery Noted or Operated On	Degree of Recovery	Age Last Follow up	Total No Injection
1	Meningitis	No	1 to 3 wk	Operation at 2½ mo	Slight	3¼ mo	89
2	Pneumonia	Yes	1 day to 4 wk	12 mo	Slight	18 mo	26
3	Prematurity	Yes	1st and 6th wk	12 mo	Slight	14 mo	2[illegible]
4	Prematurity	Ye	1 day	7¼ mo	Slight	10 mo	5
5	Prematurity	Yes	1 to 3 wk	6 mo	Moderate	13½ mo	12
6	Staph pneumonia	No	1 day to 4 wk	3 mo	Slight	3 mo	104
7	Infected pulmonary cyst	No	12 wk	9½ mo	Moderate	36 mo	40
8	Pneumonia	No	5 to 8 wk	1[illegible] mo	Slight	21 mo	[illegible]
9	Pharyngitis	Yes	16 wk	[illegible] mo	Good	11 mo	1
10	Infectious diarrhea	Yes	10 wk	[illegible] mo	Moderate	[illegible] mo	10
11*	Maternal amnionitis	Yes	1 5 days	Operation at 3 mo	Slight	2 wk postop	32
12*	Infectious diarrhea	No	2 yr	Operation 2 1/12 yr later	Slight	2 wk postop	1

* Patient in whom nerve was surgically explored and neurolysis was performed

Lack of Recovery and Management

A summary of the 12 cases prompting this report is outlined in table 1 This includes the rationale for the injections, their total number, the age at which injections were administered, the age at which recovery began, the degree of motor recovery, and the length of time that has elapsed since the injury

Recovery has been disappointing in all except case 9, an infant who had received a single intragluteal injection of penicillin, exact type unknown, at 4 months of age The residual paralysis and deformity is the most serious feature of the nerve injury, particularly in infants 2, 3, 4, and 8 who remain severely disabled 8 to 30 months after injury Infant 7 did not have severe paralysis, two and one-half years later she has weakness of calf musculature, a smaller foot, and limps when she walks Infant 6 has shown considerable improvement recently, but several important muscles remain paralyzed and foot deformity persists It is still too early to evaluate the effect of neurolysis[3] in the three patients treated surgically (cases 1, 11, and 12) There has been some recovery in the brief postoperative period A recent message from the aunt of infant 5 indicates that at 15 months of age the injured foot appears normal Improvement in her condition began at six months of age when she was first able to move her foot well However, since she has not stood unsupported or attempted walking, this information concerning her recovery is too inexact to be listed in table 1 Infant 10 has been lost to follow-up since nine months of age

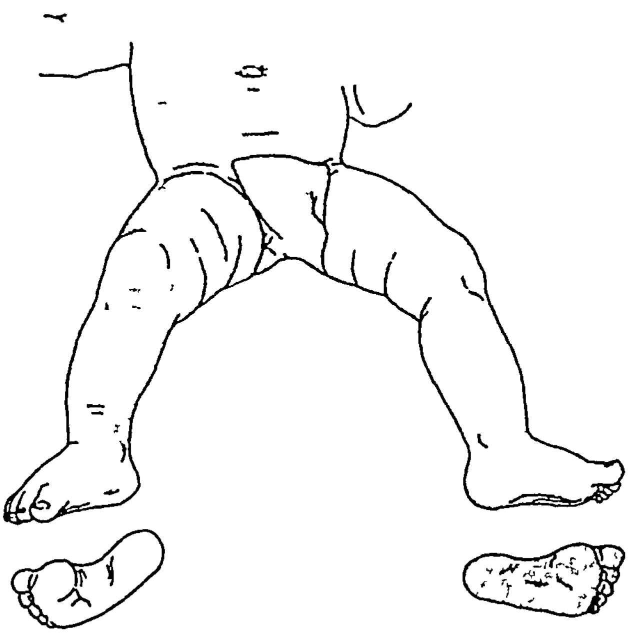

Fig 3—Sensory and autonomic deficit in area supplied by sciatic nerve, right sciatic nerve injury Sweat pattern test of patient in case 1 White, nonstippled, skin of right lower leg and foot, including sole, anhydrotic Color developed on sweating elsewhere in area from waist down where iodine starch was applied

Partial or complete anhydrosis in the sciatic nerve distribution remained in four infants tested five weeks to three months after injury Sensation has returned partially in all cases, and to a satisfactory extent in those observed as long as a year after injury

From the material available, both in the current series, in four infants previously reported[4] and in adults,[5] only a few comments regarding treatment can be offered First, early recognition of the nerve injury is of maximum importance to allow the institution of measures to prevent or minimize contractures before muscle imbalance produces fixed deformities To facilitate early diagnosis, sweat pattern testing may confirm the findings of the sensory examination, by demonstrating anhydrosis in the peripheral distribution of the sciatic nerve When the paralysis is partial, testing for functional muscle groups is necessary to make the diagnosis of motor deficit before atrophy is marked

Treatment includes early and continued maintenance of passive correctability of the involved foot by holding casts or by appropriate splints and manipulation Irrespective of the eventual degree of motor return, the prevention of fixed or static deformities of the foot and leg is of major importance Once the condition is corrected, the foot and ankle should be kept flexible by passive manipulation The parents should be warned that minor injury to the anesthetic and paralyzed foot may result in substantial lesions that heal slowly

Surgery in our and others' series[5] has invariably disclosed scarring about the sciatic nerve This scarring undoubtedly contributes to the continuation of neurological deficit, thus neurolysis would seem indicated However, longer postoperative follow-up will be necessary before definitive statements can be made regarding the value of neurolysis in promoting clinical recovery

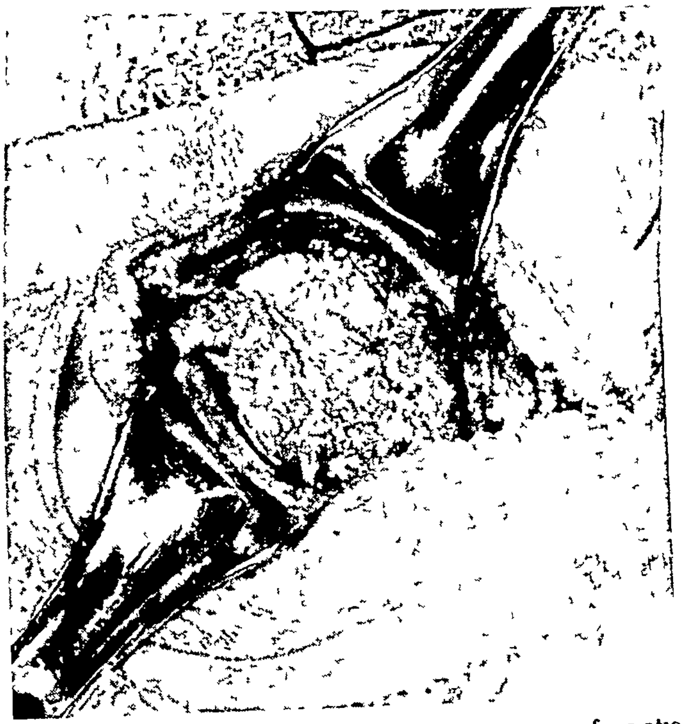

Fig 4—Photograph showing initial exposure of sciatic nerve in upper thigh of patient in case 1 Note, junction of grossly damaged and normal appearing distal nerve segment

Comment

Injection into the dangerous area of the inferior buttock is more likely to occur in infants and young children The total gluteal region is small and shallow, the patient is often squirming and uncooperative Finally, the infant is unable to report any symptoms during or after injection Figure 5 gives striking indication of the tiny area of the upper outer quadrant in a premature infant, little more than the circumference of a dime

It is important to realize that many factors may be involved in the production of sciatic nerve injury by injection The site, the volume, and the character of the injected material all participate Obviously, the smaller the infant, the greater the chance that these several factors may combine to deliver the insult Table 2 indicates the agents given in the buttock in each infant and tabulates how many infants received each agent It should be emphasized that a 4-month-old and a 2-year-old child received a single injection yet each sustained severe sciatic injury Thus, multiplicity of injections is not a necessary prerequisite for nerve injury All injections were administered by physicians or nurses with considerable training and experience No one dealing with infants should remain unaware of this problem

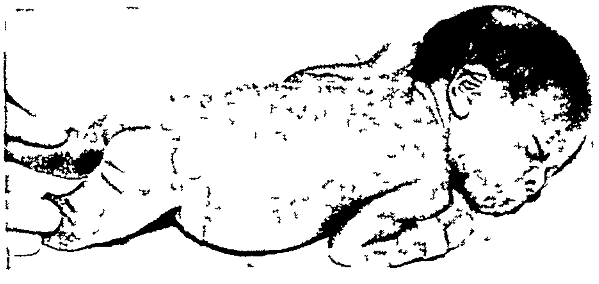

Fig 5—Shallow upper outer quadrant area of right buttock is indicated by dime on 3 lb (1,361 Gm) premature infant Sciatic nerve is in close proximity to this intragluteal injection site in small infant

Table 2—*Number of Intramuscular Injections via the Buttock in Twelve Infants*

Agent Administered	Case No 1	2	3	4	5	6	7	8	9	10	11	12	Total Patients Receiving Agent
Tetracycline		16	12	5*	6	4	28	80		10*	16	1*	10
Penicillin	24†		8‡			27†	18†		1*		8‡		6
Chloramphenicol	30§	10						2					3
Streptomycin	3‡										8		2
Vitamin K	1	1			1								3
Iron dextran			[illegible]		5								2
Gamma globulin		2											1
Caffeine sodium benzoate		3											1
Digitoxin						9							1
Promazine								1					1
Antipertussis rabbit serum								2					1

* Indicates sole drug given
† Indicates regular penicillin
‡ Indicates procaine penicillin
§ Indicates chloramphenicol succinate

Prevention

More important than the treatment of the sciatic nerve injury when it occurs is its prevention The indiscriminate use of intramuscular injections in infants and small children is to be thoroughly condemned The preferred site of injection when the intramuscular route must be used, should be the midanterior aspect of the thigh, with the quadriceps muscle as the recipient area This affords a greater muscle mass (fig 6) free of major vessels and motor nerves The instruction and supervision of all personnel giving injections should be regarded as the responsibility of the physician By use of the midanterior thigh site for intramuscular injection, sciatic nerve injuries and their serious sequelae can be avoided

Summary

Twelve infants had serious preventable sciatic nerve injury Persistent paralysis and sensory and sweating loss in the lower leg and foot followed one or more intramuscular injections in the buttock

The midanterior thigh is recommended as the preferable site for intramuscular injections in infants and young children

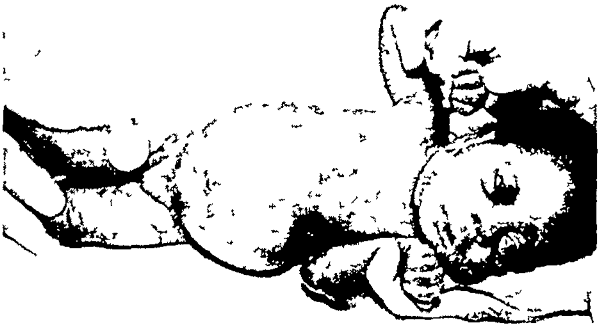

Fig 6—Location of coin indicates preferable site for intramuscular injections Midanterior thigh recommended in infants and young children In same infant pictured in figure 5, area greater than that included under quarter is available

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AN APPROACH TO THE TEACHING OF FAMILY CARE

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In the program here outlined each junior-senior pair of medical students provides comprehensive medical care to two families Under the supervision of a health team the student follows these families in health and disease for the entire two years of his clinical training The program is intended to demonstrate, in a general practice setting, the influence of environmental factors upon health, to encourage the team spirit in the solution of health problems, to introduce the student to the resources in the community, and to demonstrate in practice the integration of preventive and curative medicine

A family care unit has been organized, under the chairmanship of Dr Leon R Lezer, as a division of the department of preventive medicine at the University of Vermont It serves as a general practice demonstration and provides students with experience in comprehensive medical care

Organization

Families—About 100 local families participate in the program These families are selected on the basis of their teaching value, which includes a wide range of medical and social diagnoses and a fair representation of each age group, from infancy to old age The group includes normal, well-adjusted families as well as those with difficult diagnostic and social problems They are medically indigent, for the most part, and at present no fees are charged for services These families understand the program to be a cooperative venture to which they contribute and from which they gain

Students—Medical students enter the program at the beginning of their junior year and continue through it until graduation Two families are assigned to each junior-senior pair of students The senior student, under supervision, has the primary responsibility for the family Each student cares for the same two families for two years Such a period allows the student to note not only the sporadic illnesses which occur but also the natural history of disease and the influences of environmental factors on the health and well-being of the family unit The experience, then, is quite different from any other which the student has either in hospitals or in the outpatient clinics It is felt that the student must be allowed such a period in order to observe the continuum of health and disease and to develop specific attitudes These are the objectives of the program

Although the student enters this program in his third year, the orientation toward it begins in the freshman year with a course in human ecology From the beginning of the student's career, he develops an appreciation of the influence of environmental factors on health, this understanding he may now apply to the study and management of a family The instruction he receives during his second year, such as clinical epidemiology, medical care, and public health may also be applied in the third and fourth years In other words, the program constitutes his clinical training in preventive medicine

In the care of his assigned family, the student has the opportunity to apply his knowledge of other major branches of medicine to the acute and chronic illnesses which occur, and he also has an excellent opportunity to develop a positive program of health for this family He learns to distinguish the well person from the sick person and to evaluate both He combines prevention, cure, and rehabilitation in the total care of the patient The student-physician here plays the role of the traditional family physician, but with the important difference of having modern facilities at his disposal in order that he may provide a higher quality of medical care in a shorter period of time He uses the offices of the department which are equipped with facilities and personnel to simulate those of a private practitioner

The student explores the resources of the community, in his care program, and frequently will establish contact with health, welfare, social, and governmental agencies He soon learns that by working with other health personnel, he can do more for his patients in a shorter period of time than by working alone In the management of the families the student-physician may exercise his role as a teacher He learns to measure the success of his teaching by the degree of active participation of his patients in their adventure of healthful living rather than their otherwise passive acceptance of medical care

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During its first year the program has included sophomore nursing students from the university, one of whom has been assigned to a family The nursing student meets the family at the time of the initial evaluation in the office, makes a visit to the home, and is present and participates to some extent when the family is discussed at seminar One senior nutrition student from the university has also spent time in the program Further exploration of teaching for nutrition students in the family care unit is currently being undertaken

Teaching—A team, consisting of a physician, a public health nurse, and a medical social worker, all full-time members of the department of preventive medicine, is responsible for teaching these students Eight general physicians in private practice in this area also devote part of their time to teaching in the program Referrals to any specialty clinic are made as the circumstances require Each house call and office visit is carefully reviewed and discussed with the student as previously indicated The teaching team has frequent discussions, apart from the students, to ensure that the family's needs are being met and that the student is using the medical, nursing, and social resources which are available In the beginning, the student is likely to ignore the healthy members of the family in accordance with the view that 'he that is well hath no need of a physician" The student also tends to focus readily on the traditional, strictly medical aspect of the patient's condition and to ignore the environmental factors It is the responsibility of the teaching team to maintain these factors in their proper perspective The student has the responsibility to make his own decisions and to exercise his own judgment in the types of situations which he will encounter in future private practice However, he always has the assurance that consultation and help are available, if necessary, at all times The teaching is therefore largely informal The students arrange their own office appointments and house calls in accordance with their academic programs Since the family care unit program is concurrent with all other studies and clerkships during the clinical years, the only sessions which are not scheduled by the student himself are the orientation sessions and the seminars This means that the student must decide on the most convenient time to answer a house call He must also decide if he will make a house call or see the patient at the office If the situation should arise in which the student is unable to contact one of the regular members of the teaching staff, he may consult with a resident physician at one of the two teaching hospitals in regard to the management of his patient

Seminars are held twice a week, and the students present the families for discussion according to a planned schedule In addition to the members of the staff, other persons who have contributed to the health of these families may be present at the family seminar Seminars have included members of the clergy, visiting nurses, teachers, social workers, and others beside the regular staff Only persons who have a direct interest in the family are invited by the students

What the Program Is Not

The program must be differentiated from the home-care programs where the objective is to provide follow-up care after hospitalization or to provide home care for persons with chronic illness This program includes both of these features but *focuses on health rather than on disease,* and the family is viewed as the basic unit Although the teaching is done in a general practice setting, the primary purpose is not to produce general practitioners Rather, it is expected that the principles taught will find application in whatever field of medicine the student may pursue The unit is not another clinic, it is the center of a program which was designed to help students understand the influence of total environment on health It is intended to teach not clinical medicine but community medicine, nor is it intended primarily to teach facts but to develop the attitudes of comprehensive medical care It is not a medical care service, but a teaching unit, with organizational potential for research

Evaluation

Although many of the expected results from such a program are intangible, there are definite results which are anticipated The student's record of curative and *preventive familial care* should be complete He is expected to show concern for his family in health and in disease The history and the physical examination of the members of the family must be adequate and the indicated laboratory work done The diagnosis should be justified Consultation must be sought whenever advisable The treatment is to be patient centered rather than directed towards a specific organ In other words, the management includes total patient care, and the student is required to use the available resources in the community for the benefit of the family The follow-up should be adequate The student is expected to work with his partner and with the other members of a health team Finally, he must demonstrate professional competence combined with a sympathetic and intellectual understanding (in the broad sense) in the care of his patient

232 S Willard St

ACUTE APPENDICITIS WITH PERFORATION

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A group of 98 patients with appendicitis with perforation was studied to determine symptoms and findings that might help predict perforation in patients suspected of having acute appendicitis Management of appendicitis with perforation is outlined on the basis of the results in this series The initial symptom was pain and tenderness in the right lower abdominal quadrant, and it occurred in 97 patients, there was nausea in 82, vomiting in 77, diarrhea in 19, and constipation in 13 Eighty-nine patients had fever, an elevated pulse rate, and an elevated leukocyte count The duration of symptoms was not informative The incidence of perforation was much higher in children than adults There were 30 patients 10 years of age or younger, and 61 were 20 years of age or younger The authors are inclined to advise immediate operation provided the patient is adequately prepared

Acute appendicitis complicated by perforation remains a serious problem and accounts for significant mortality and morbidity in the nation each year Many times the diagnosis of acute appendicitis is difficult to make It is the purpose of this paper to define, by analysis of a group of cases which progressed to perforation, some of the symptoms and findings which may help to predict impending perforation in patients who are suspected of having acute appendicitis and to discuss the management of perforated appendicitis based on the results of this series

Ninety-eight patients who had perforated appendix were treated on the wards of Roper Hospital from January 1950 to January 1959 There were 71 male patients and 27 female patients The youngest patient was 18 months of age and the oldest 80 years of age There were 30 patients 10 years of age and younger Sixty-one were 20 years of age and younger Most of the patients were indigent and were attended by numerous attending and resident surgeons Twenty-four patients had received some form of cathartic prior to admission A preoperative diagnosis of acute appendicitis was made in 92 patients The other preoperative diagnoses included low colon obstruction, carcinoma of the cecum, cyst of the ovary, ruptured viscus, strangulated bowel obstruction, and ruptured peptic ulcer

Symptoms and Findings

The initial symptom was abdominal pain in 84 patients The textbook pattern of pain beginning in the umbilical area and moving to the right lower abdominal quadrant occurred in only 11 instances Most frequently pain began in the right lower quadrant of the patient's abdomen and remained there Regardless of the initial location, the pain localized to the right lower quadrant in 60 patients and to the lower abdomen in 11 patients The frequency with which symptoms occurred was as follows pain in 97 patients, nausea in 82, vomiting in 77, diarrhea in 19, and constipation in 13

Forty-four patients had symptoms which lasted for only 48 hours or less The 40 patients who were 12 years of age and under had an average duration of symptoms of 3 5 days The remainder had an average duration of symptoms of 3 8 days

Tenderness in the right lower abdominal quadrant was found in 97 patients Rebound tenderness occurred in 70, voluntary guarding in 75, and true muscle spasm in 59 patients Oral temperature above 100 F (37 8 C) was found in only 62 patients Fifty-two patients had a pulse rate of more than 100 per minute White blood cell counts were greater than 10,000 per cubic millimeter in 81 patients

Treatment

Immediate operation was carried out on 93 patients The primary operation was appendectomy in 81 patients, appendectomy with appendicocecostomy in 11, and drainage of appendiceal abcess in 1 A secondary operation of drainage of pelvic abcess was performed in 7 patients, release of small bowel obstruction in 1, and drainage of wound abscess in 1

There were five patients who were not operated on initially One of these was an extremely obese, diabetic, mentally defective patient who had been admitted with a history of diarrhea of five days duration She became semi-comatose in 18 hours after admission and died on the fourth day of hospitalization Four patients who had appendicitis

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Assistant Professor of Surgery (Dr Bradham), Professor of Surgery and Chairman of the Department of Surgery (Dr Kredel), and Second-year medical Student (Mr Green), Medical College of South Carolina

with abscess formation in the right lower abdominal quadrant were not operated on initially but were treated conservatively One of these died on the second day of hospitalization Autopsy revealed a perforated appendix and generalized peritonitis Hemorrhagic pericarditis and pulmonary edema were also found The other three patients responded well to this program All were advised to return for interval appendectomy One followed instructions and had an uneventful appendectomy six weeks later One sustained another acute attack, was operated on, and found to have acute appendicitis with perforation He recovered satisfactorily The third patient in this group has not been heard from since discharge

In addition to the patients who had secondary operations for complications, there were several other patients readmitted with recurrent fever and a tender mass in the pelvis which was not fluctuant These responded well to antibiotic therapy Another significant complication was the pulmonary embolus which occured in a patient one day postoperative and is discussed later

Of the 93 patients operated upon primarily, 30 patients received intraperitoneal antibiotics and 63 did not For those who received antibiotics in the peritoneal cavity at operation, the average duration of a febrile course postoperatively was 5 days, and the average duration of hospitalization postoperatively was 11 7 days Three patients (10%) had a postoperative complication For those who did not receive intraperitoneal antibiotics the average postoperative febrile period was 7 1 days and the average duration of postoperative hospitalization was 12 8 days Eight patients (12 7%) had a complication postoperatively Penicillin and streptomycin in various combinations, strengths, and irrigating solutions were used in 23 cases Penicillin alone was used in two cases, streptomycin alone in one case, terramycin in three cases, and sulfonamide crystals in one case

Cultures of either the peritoneal fluid or pus were reported in the majority of cases These combined with antibiotic sensitivity studies were used as a guide to antibiotic therapy Most were mixed infections Escherichia coli was the predominant organism in 27%, Aerobacter aerogenes in 17%, and alpha hemolytic streptococcus in 13% of the cases in which cultures were obtained and reported The remaining cultures included a wide variety of organisms as the predominant one on culture

Mortality

Four patients died, giving an over-all mortality of 4 1% Two of these were in the nonoperative group and have been mentioned previously The third patient was a 40-year-old man who died on the first postoperative day A clinical diagnosis of pulmonary embolism was made Permission for an autopsy was not granted The fourth patient was admitted with a history consistent with acute appendicitis for five days Appendectomy and drainage of a retrocecal abscess was performed on the day of admission The postoperative course was relatively stormy until the sixth day when his temperature rose to 105 F (40 6 C) and he died A urine for porphyria was 3+ Autopsy revealed an abscess in the retrocecal area, an infected wound, sicklemia, and generalized arteriosclerosis

Comment

As with any other disease, acute appendicitis with impending perforation will occasionally follow an atypical pattern In this series of 98 patients with perforated appendicitis, 97 gave a history of abdominal pain and had tenderness in the right lower abdominal quadrant when examined on admission Eighty-two were nauseated and 77 had vomited Eighty-nine patients had fever, an elevated pulse rate, and an elevated leukocyte count These symptoms and findings, therefore, appear to be dependable criteria for making the diagnosis of appendicitis with perforation or for following patients in which the diagnosis is doubtful The duration of symptoms in this series was not a reliable factor as 44 patients had symptoms less than 48 hours prior to admission Duration of symptoms in appendicitis varies considerably and should not replace clinical evaluation of the patient In this series, the children did not seem subject to earlier perforation than the adults In reviewing all of our cases of appendicitis the incidence of perforation was much higher in children than in adults however For this reason and because of the severe nature of this disease in children, Gross [1] strongly opposes the nonoperative treatment of children with peritonitis of appendiceal origin but considers a short period of preparation highly important in the care of the desperately ill subject Rees [2] decries conservative treatment for appendicitis in all age groups

There was no set policy regarding operative or nonoperative therapy No comparison can be made between results of either method of management as there were only five patients who did not have an operation It was not possible from available data to accuratey divide these patients into those having localized peritonitis localized abscess formation, or diffuse peritonitis

The five patients not operated on exemplify several interesting and very practical considerations One patient was admitted in an almost moribund condition Diagnosis was not established because of the patient s inability to communicate and her extreme obesity It became a matter of surgical judgement whether to subject this patient to operation It was the opinion of those in attendance that operation would not be tolerated This type of patient cannot be automatically placed in the operative therapy group Another patient who was thought to have localized abscess formation died two days after admission and was found to have generalized peritonitis This case clearly points out the difficulties of classifying these patients too closely and employing therapy accordingly Another patient promptly developed acute appendicitis again after discharge from the hospital and when operated on, the appendix was found to be perforated Another patient did not keep the appointment for appendectomy The courses followed by these latter two patients can be anticipated in many of our indigent patients

The controversy over operative and nonoperative management of appendicitis with generalized peritonitis is clearly stated in "Current Surgical Management"[3] Both methods of therapy and the rationale for selection are outlined Hawk, Becker, and Lehman[4] studied 1,003 cases of appendicitis at the University of Virginia Hospital over a 10-year period and found that immediate operation resulted in mortality, mean number of complications, and mean duration of hospitalization which was one-half that obtained with conservative management The number of those treated conservatively, however, was too small to be statistically valid They, as well as Bothe who discussed their paper, found difficulty in distinguishing preoperatively between localized disease and generalized peritonitis In further discussion of this paper Lanman cited a high incidence of perforation in children and Parsons cited a high incidence of perforation in patients 60 years of age and older

Those who advocate nonoperative management clearly define the type of case in which this form of therapy is used Ochsner and Johnston[5] used conservative treatment for appendiceal peritonitis in only those cases in which localization of the infective process had taken place These authors described the difficulty in determining this at times and believed that unless there was definitely a palpable mass indicating localization, exploration is probably indicated When abscesses developed, they were drained Guerry and McCutchen[6] employed the conservative program for those patients who had diffuse peritonitis It was their experience that cases with diffuse peritonitis would progress to localization if they could be carried through the phase of diffuse peritonitis As soon as localization was established, operation was performed Two series of patients with acute, gangrenous, ruptured appendicitis with diffuse peritonitis were compared Immediate operation in 94 cases resulted in 10 deaths (10 64% mortality) Deferred operation in 139 cases resulted in two deaths (1 45% mortality) They regarded the deferred treatment as the first step in the operative procedure and not as a substitute for operation In final analysis, well-stated by Guerry and McCutchen,[6] "there is an optimum time for operating upon every surgical patient The great problem of surgical judgment is to be able to select that time"

In our own cases, we are inclined toward immediate operation provided the patient has been adequately prepared If the need for fluids, electrolytes, blood, and digitalization are more important than the delay their administration would cause, then, of course, operation is delayed for the necessary period of time If a frank abscess is encountered and the appendix cannot be removed without breaking down the walling off defenses, the abscess is drained extraserously if possible and an interval appendectomy is carried out six to eight weeks later In all of our patients operated on, except one, the appendix was removed Appendicocecostomy is used when conditions are unfavorable for satisfactory closure of the appendiceal stump as described by Prioleau[7] The peritoneum and fascia are closed The skin and subcutaneous tissues are packed open to be closed in two or three days secondarily Gastrointestinal intubation is continued until peristalsis is established Postoperative antibiotics consisting of penicillin and streptomycin are given until all signs of infection have abated Intraperitoneal antibiotics are not used routinely

Summary

A series of 98 patients who had acute appendicitis with perforation treated on the wards of the Roper Hospital from January, 1950, to January, 1959, are presented An analysis was made to determine the most frequent symptoms and findings associated with this disease The most effective means of treatment in our hands, based on the results in these cases, is given The four patients who died were discussed briefly Two of these were in the operative group and two were in the nonoperative group Several factors to be anticipated in nonoperative treatment of acute appendicitis with perforation are brought out by this study The rationales of both the operative and nonoperative methods of management are discussed

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HYPERADRENOCORTICISM

REVERSIBILITY OF PHYSIOLOGICAL AND CLINICAL CHANGES ASSOCIATED WITH EARLY HYPERADRENOCORTICISM TREATED BY TOTAL ADRENALECTOMY

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Eighteen patients were treated for hyper adrenocorticism during its early stages by total adrenalectomy In 14 of the patients the most significant problem before operation was cardiovascular deterioration, 9 of them had hypertension and 5 had congestive heart failure The other four patients were women with progressive masculinization Time elapsed since adrenalectomy varied from 12 to 35 months The most significant improvement was the arrest of progressive cardiovascular damage All patients demonstrated a decrease in osteoporosis, weakness was improved in all but four, and only one patient continued to demonstrate the "moon face" There have been six episodes of addisonian crises These were recognized early and treated adequately All but one patient showed marked subjective improvement, especially a decrease in nervousness and emotional lability There has been a significant reduction in hirsutism in the female patients The long term follow up data on these 18 patients indicate the feasibility of total adrenalectomy for hyperadrenocorticism in the early stages

Adrenalectomy is currently performed for treatment of adrenal cortical hyperfunction, hypertension, and the palliation of a variety of malignant diseases There are few long-term follow-up studies on significant numbers of patients to appraise the reversibility of the pathological physiology in these disease states Malignant disease, which comprises the largest number of patients, by its very nature precludes their use in general long-term appraisals Although most of the currently available observations on patients with iatrogenic adrenal cortical hypofunction have been secured from this latter group of patients, no example of preoperative adrenal overactivity was available for comparison There are several relatively large series of hypertensive patients treated by adrenalectomy, but selection and follow-up of most patients proceeded purely on the basis of their hypertension Preoperative determinations of adrenal activity and its function in these patients deranged physiology were not commonly used in either their selection or appraisal Detailed studies of patients with adrenal cortical hyperfunction subjected to adrenal ablation are available, but in relatively small series and generally only in the advanced state of the disease

It has been our observation, and that of others, that many of the degenerative sequelae of long-standing hyperadrenocorticism, e g, hypertensive cardiovascular disease, osteoporosis, and diabetes, are not reversible Since we have had occasion to follow the progress of a number of patients treated in an earlier phase of this syndrome, we thought it worthwhile to present their current status Accordingly, this report is concerned with the chronic postoperative status of 18 patients treated for hyperadrenocorticism by bilateral adrenalectomy[1] The indications for surgery and the preoperative data on these patients, most of whom were in the early stages of adrenocortical hyperfunction, have been reported previously[2]

In 14 of the 18 patients the most significant problem was that of cardiovascular deterioration There were nine patients with hypertension and five with congestive heart failure The remaining four patients were women whose primary problem was progressive masculinization The time elapsed since adrenalectomy varied from 12 to 35 months Two deaths occurred in this group—one 9 and the other 12 months after operation during episodes of congestive heart failure

These patients were examined clinically as to their physical and mental condition, and biochemically with observations of their blood levels of sodium, potassium, chloride, carbon dioxide combining power, uric acid, urea nitrogen, calcium, phosphorus, and hematocrit Urinary sodium, potassium, chloride, calcium, and phosphorus excretion rates also were determined

Results

Preoperative data are included in tables 1 and 2 for comparative purposes Table 1 shows the improvement in the cardiovascular findings of these patients about 20 months (average) after adrenalectomy Significant improvements in the appearance of fundi, cardiothoracic ratio (from 45 to 38), and electrocardiographic changes were noted in all patients Concurrent decreases in blood pressure (from 161/107 to 119/87 mm Hg), body weight (from 209 to 167 lb [94 8 to 75 7 kg]), and edema also were observed It should be noted that pre-

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From the departments of medicine and surgery Baylor University College of Medicine operatively (P) the blood pressure of the patients in cases 4 and 10 was within normal limits, but during a state of maximum antihypertensive therapy with diuretics, rauwolfia alkaloids, and mecamylamine hydrochloride The current (C) reading is not related to antihypertensive therapy

Table 2 compares other findings, concomitant with hyperadrenocorticism prior to adrenalectomy, with current ones All patients demonstrated a decrease in osteoporosis Weakness was improved in all but four patients who had had this complaint previously Only one patient continued to demonstrate the "moon face" associated with hyperadrenocorticism In five of the patients with menstrual problems normal menses have been restored, and one of these has since become pregnant and delivered a normal child Marked improvement in emotional stability was noted in eight patients, while five showed moderate improvement Three patients exhibited no change

In comparing the preoperative biochemical status with that currently observed, there were no significant changes in blood urea nitrogen, serum sodium, calcium, or carbon dioxide contents Slight changes were an increase in the average levels of serum potassium (from 3 8 to 4 8 mEq per liter) and of serum phosphorus (from 3 0 to 4 8 mg %) and decreases in the levels of serum chloride (from 97 to 89 mEq per liter) and uric acid (5 3 to 4 4 mg %) Hematocrit readings and blood volumes remained within normal limits Of the urinary electrolytes (sodium, potassium, chloride, calcium, and phosphorus) only sodium and chloride showed an increase in excretion over normal limits, sodium excretion being 244 mEq per 24 hours and chloride excretion 141 mEq per 24 hours The sodium-potassium ratio was 4 1

Comment

Observations on this number of patients (18) within a three-year period implies an incidence above that generally accepted for adrenal cortical hyperfunction The clinical and biochemical status of these patients, however, was most consistent with hyperadrenocorticism In all patients presenting with menstrual disorders a complete gynecologic check-up and a minimum of three months' therapy with hydrocortisone or fludrocortisone acetate (9-alpha-fluoro-17-hydroxycorticosterone-21-acetate) was without benefit Since the conditions of this group of patients could not be adequately controlled medically, especially in terms of cardiac competence, they were subjected to total adrenalectomy

Since performance of adrenalectomy, the most significant improvement noted in these patients has been the arrest of progressive cardiovascular damage, as seen by funduscopic changes, relief of hypertension, improved electrocardiographic findings, and relief of congestive heart failure This early arrest of damage is the most vital aspect of treatment and, even though adrenalectomy is a radical procedure, it must always be considered when the patient has separately, alternatively, or in combination hypertension, diabetes, osteoporosis, and clinical and laboratory evidence of adrenal hyperfunction and does not respond to maximal medical therapy

These patients are maintained at this time on as low a steroid replacement dosage as possible, concurrently with a high-salt diet The hydrocortisone replacement dosages range from 0 to 30 mg per day, with an average of 15 mg per day It is believed that this adequately prevents hyperpotassemia and allows these patients adequate remission from their disease with safety The daily salt intake averages about 20 Gm The only significant observation relative to this program is an increase in urinary sodium excretion and a tendency toward addisonian pigmentation Even with such a large urinary sodium output, there is no concomitant change in serum electrolyte values Therefore, we

TABLE 1 —*Cardiovascular Findings in Eighteen Patients Treated by Adrenalectomy*

	Findings*												Time Since Surgery Mo
	Blood Pressure Mm Hg		Weight lb		Edema		Fundi		Cardio/Thoracic Ratio		ECG		
Case, No	P	C	P	C	P	C	P	C	P	C	P	C	
1	160/110	118/84	167	131	0	0	0	0	40	34	N	N	21
2	150/100	130/96	226	212	4	1	2	1	47	43	3	N	33
3	110/80	120/78	120	120	0	0	0	0	42	39	N	N	21
4	170/90	150/108	187	163	3	1	3	1	46	44	2	2	12
5	160/70	112/60	220	160	2	0	0	0	45	32	1	N	18
6	150/100	110/80	158	120	1	0	0	0	54	35	2	N	23
7	180/120	110/70	190	131	2	0	2	0	38	36	2	N	22
8	160/100	98/60	180	115	1	1	1	0	42	33	N	N	18
9	170/110	120/80	218	194	4	2	4	1	44	42	N	N	16
10	160/80	140/90	292	226	4	0	2	1	49	39	1	N	16
11	200/120	110/80	301	201	4	0	3	1	48	37	3	1	35
12	200/120	100/80	180	171	3	0	3	1	46	43	3	2	18
13	190/110	100/70	178	135	1	0	2	0	48	35	3	N	22
14	165/110	120/85	203	157	2	1	2	0	43	39	2	1	18
15	184/120	150/100	300	215	3	3	2	0	50	40	2	N	15
16	200/130	126/80	230	172	2	0	2	1	45	38	2	N	15
17	150/110		201		2		3		46		2		18
18	250/140		220		4		3		50		4		15
Average	161/107	119/87	209	167	2 3	0 5	1 8	0 4	45	38	1 8	0 3	20

* P = preoperative status C = current status Edema is graded 0 to 4 plus Funduscopic gradings Keith Wagner classification (14) ECG grading grade 4, hypertrophy of left ventricle with strain and ischemia, grade 3 hypertrophy of left ventricle with strain grade 2, hypertrophy of left ventricle without strain, and grade 1, minimal T wave changes only N = normal

have not considered it necessary to add fludrocortisone acetate to the therapeutic program However, this program may not be optimal in all cases When there is a history of marked and prolonged congestive heart failure, a low-salt high-steroid therapeutic program is needed to obtain maximum relief from the congestive failure

The two deaths in this series were due to prolonged intractable congestive heart failure Although the conditions of both patients were somewhat improved after the operation, they had only a temporary remission (9 and 12 months, respectively) from a long history of congestive heart failure which, during an exacerbation, led to a terminal state

There have been six episodes of addisonian crisis among the 18 patients All were recognized early and promptly treated adequately, generally by increasing orally given doses of hydrocortisone 5 to 10 times

All but one patient reported marked subjective improvement, especially a decrease in nervousness and emotional lability There has been a significant reduction in hirsutism in the female patients, although at a much slower rate than the relief from hypertension and congestive failure

Summary

The long-term follow-up data on 18 patients in the early stage of hyperadrenocorticism who were treated with total adrenalectomy indicate the feasibility of definitive therapy for this disease, which otherwise usually produces devastating effects

2002 Holcombe Blvd (31) (Dr Ford)

TABLE 2—*Other Findings of Hyperadrenocorticism in Eighteen Patients Treated with Bilateral Adrenalectomy*

Case No	Osteoporosis P	Osteoporosis C	Weakness P	Weakness C	Hirsutism P	Hirsutism C	Moon Face P	Moon Face C	Menses† P	Menses† C	Emotional Instability P	Emotional Instability C
1	2	0	4	1	4	0	4	0	A	N	4	3
2‡	4	2	4	1			4	1			3	N
3	0	0	4	2	3	0	1	0	M	N	4	1
4‡	0	0	2	2			3	0			2	1
5	1	0	4	0	4	0	4	0	A	N	3	1
6	4	2	4	4	1	0	4	0	A	A	2	3
7	2	0	4	1	2	0	1	0	N	N	3	1
8	1	0	4	1	4	2	3	0	O	P	2	N
9	2	1	4	4	4	2	4	0	C	C	4	2
10	1	1	4	4	1	0	4	0	O	O	3	3
11	2	1	4	0	1	0	4	0	N	N	2	N
12	2	1	4	4	1	0	2	0	C	C	2	3
13	2	1	4	3	2	0	4	0	O	N	2	1
14	1	0	3	1	1	0	4	0	N	N	3	1
15	2	0	4	0	1	0	4	4	O	O	3	N
16	2	0	4	0	4	0	4	0	O	O	4	3
17	1		4		2		4		O		2	
18	2		4		4		4		A		3	

* Osteoporosis, weakness, hirsutism, moon face, and emotional instability are graded 1 to 4 Grade 4 is an extremely marked condition, grade 3 a significantly noticeable condition, grade 2 moderate, and grade 1 slight P = preoperative C = current

† M = menorrhagia N = normal A = amenorrhea O = oligomenorrhea P = pregnant C = climacteric or menopause and H = hysterectomy

‡ Male patients

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CLINICAL NOTES

UNTOWARD EFFECTS FROM SKIN GRAFTS

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An autogenous skin graft may regenerate in all its parts if the 'take" is complete In this manner the missing eyebrow can be replaced with a hair-bearing full-thickness graft from the scalp Some of the hair may fall out after the transplantation, but the surviving hair follicles will again grow hair of the same quality and in the same direction as it grew on the donor area If the hair growth on a skin graft is unintentional however, this can become embarrassing Hence skin grafts to be used for lining cavities such as the eye socket, buccal sulcus, or vagina, and for replacement of skin of other hairless regions, should not only be taken from a hairless region of the body but the donor area should not be shaved preoperatively This lesson was learned from the experience with the following cases

Report of Cases

CASE 1—A large full-thickness graft was taken from the abdomen in the repair of a burn contracture of the palm and all fingers The abdomen and pubic area were shaved preoperatively, since the patient (male) had a fair complexion, the borderlines of the two areas were not readily discernible, and it happened that part of the donor site lay within the pubic area The graft 'took' almost completely, and some curly hair grew on the hypothenar eminence later it was removed by electrolysis

Case 2—This example demonstrates the consequences of a different type of error in the selection of donor areas of skin grafts A 5-year-old boy sustained extensive third degree burns of both lower extremities and the right side of his face, including the ear Both legs were covered with skin grafts in five operations The grafts were taken from the abdomen, chest, and back The abdominal donor areas were used twice All grafts "took" reasonably well, one so well that it caused some consternation when the boy was seen again 15 years later He returned at that time for reconstruction of the partially missing right ear

A follow-up examination of the grafted areas of the lower extremities revealed a fully grown, dark brownish pigmented nipple and areola on the median side of the left calf (fig 1) and a scar at the original nipple site on the left side of the chest wall, from which one of the skin grafts had been taken During one of the reconstructive operations on the ear, the areola was excised from the calf and returned to its "home base" at the left side of the chest after excision of the scar in this area (fig 2) The surface defect on the calf was covered with a split-thickness skin graft from the thigh

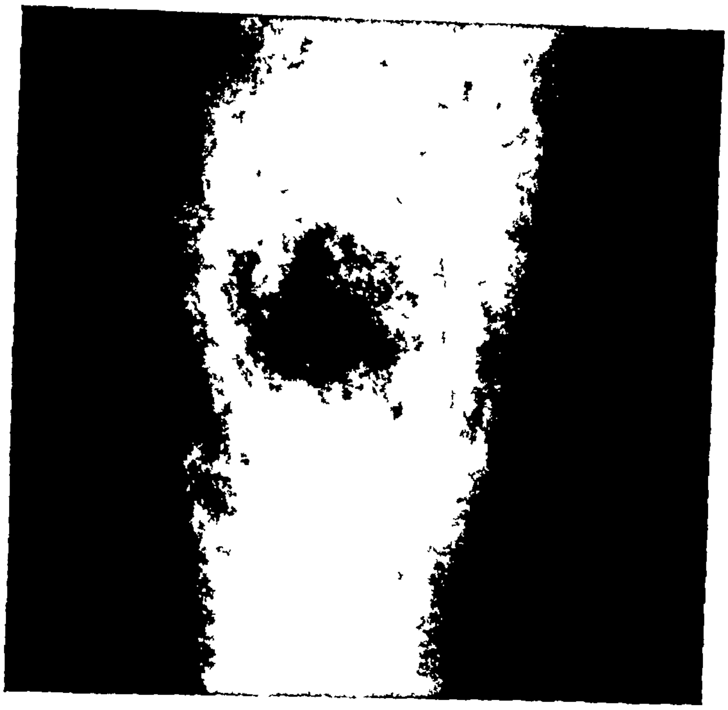

Fig 1 —Photograph of median side of left calf of 20-year-old patient on which 15 years previously, during burn treatments, a split skin graft from the left chest wall had been transplanted Graft was cut thicker than intended and contained left aerola which "took" and grew

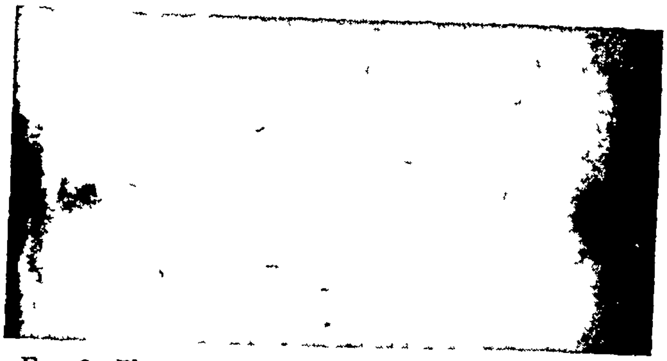

Fig 2 —Photograph of same patient's chest, after return of areola as a graft from calf to left side of chest wall

255 S 17th St (3)

ORCHITIS AS A COMPLICATION OF INFECTIOUS MONONUCLEOSIS

Lloyd S Ralston, M D, Arthur K Saiki, M D
and
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Infectious mononucleosis is a common disease occurring mostly in the younger age groups The disorder is well known for its protean manifestations This report describes a complication, orchitis, which to our knowledge has not been previously reported

Report of a Case

A 29-year-old man was admitted to Deaconess Hospital on March 1, 1959, having noted the onset of general malaise two weeks before admission One week later he suddenly developed chills, followed by fever, profuse sweating, and a severe frontal headache The patient retired to bed at home where the paroxysm of chills and fever recurred several times daily, associated with a severe frontal headache, a dry, nonproductive cough, gradual loss of appetite, diarrhea of five to six semiformed, clay-colored stools daily, and excessively dark urine Four days before admission his testes became sore, and over the succeeding three days they became grossly swollen and so tender that he could barely walk On the day of admission he developed a sore throat and "swollen glands" in the neck

Physical examination revealed an acutely ill man The blood pressure was 138/80 mm Hg, pulse rate 104 per minute, and temperature 101 4 F (38 6 C) The sclera were grossly icteric The patient's pharynx was intensely red and edematous, and small areas of exudate were noted in the right tonsillar area The neck was supple, with many pea-to-walnut-sized, nontender lymph nodes palpable in both posterior cervical triangles His liver was palpable 3 to 4 fingerbreadths below the right costal margin on deep inspiration and was slightly tender The spleen was not palpable Both testes were swollen to the size of a small orange and tender

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From the departments of medicine and pathology, University of North Dakota School of Medicine, the Grand Forks Clinic, and the Valley Medical Associates to touch There was neither scrotal redness nor was there warmth noted on palpation

Admission laboratory examinations revealed a hemoglobin concentration of 15 5 Gm per 100 cc, red blood cell count 4,720,000 per cubic millimeter, and white blood cell count 5,000 per cubic millimeter Examination of the peripheral blood smear showed a differential count of 1% eosinophils, 1% stabs cells, 18% segmented neutrophils, 78% lymphocytes, and 2% monocytes The lymphocytes exhibited Downey type I and type III cells consistent with a diagnosis of infectious mononucleosis Heterophil antibody was present in 1 3,584 dilution (guinea pig absorption) Agglutination was absent for typhoid O, typhoid H, paratyphoid B, and brucellosis bacteria Serologic findings were negative Urinalysis showed a specific gravity of 1 022, a faint trace of albumin, no sugar or acetone, and was positive for bile (Ictotest) Microscopic examination of the urinary sediment showed only an occasional hyaline cast Serum bilirubin level was 1 2 mg direct and 2 8 mg total per 100 cc, cephalin flocculation 3+ in 24 and 48 hours, thymol turbidity 2 8 units, sedimentation rate 13 mm per hour (Westergren), and alkaline phosphatase level 7 4 Bodansky units per 100 cc Lactic dehydrogenase level was 985 units (normal 200-680 units), serum glutamic oxalacetic transaminase (SGO-T) activity 135 units (normal 8 40 units), and serum total protein level 7 7 Gm% per 100 cc, with 4 48 Gm% albumin and 3 2 Gm% globulin Chest x-ray revealed no abnormalities

The patient was placed at bed rest, given a general diet, and treated with 10 grains of aspirin every four hours Codeine ½ grain was given orally for the headache The scrotum was supported with perineal padding, and cold applications were administered

During the first 10 hospital days the patient remained ill His temperature was continuously elevated in the range of 100 to 101 F (37 8 to 38 3 C) His appetite was poor, and he complained of generalized muscular aches and pains On the 11th hospital day the temperature returned to normal and his condition immediately began to improve The testicular swelling and tenderness abated rapidly, his appetite returned, icterus was no longer evident, and the liver was just palpable at the right costal margin and only slightly tender Three weeks after admission the results of urinalysis were normal Heterophil antibody was present in 1 1,792 dilution (guinea pig absorption 1 896 dilution), sedimentation rate was 5 mm per hour (Westergren), and serum bilirubin level 0 3 mg% direct and 1 2 mg% total per 100 cc The serum total protein level was 7 7 Gm% per 100 cc fractionated to 4 4 Gm% of albumin and 2 3 Gm% of globulin He was released from the hospital 28 days after admission feeling well

The patient did well after discharge from the hospital His only complaint was of a vague ache in both testes which disappeared after two months On June 1, 1959 (three months after onset), results of laboratory tests were as follows urinalysis completely normal, hemoglobin concentration 17 1 Gm per 100 cc, and white blood cell count 6,100 per cubic millimeter, with a differential count of 31% lymphocytes, 58% polymorphonuclear cells, 2% eosinophils, 8% monocytes, and 1% basophils No Downey cells were seen Bilirubin level was 0 15 mg direct and 0 4 mg total per 100 cc, other values were alkaline phosphatase 1 35 Bodansky units per 100 cc, acid phosphatase 2 1 King-Armstrong units per 100 cc, and sulfobromophthalein 1 6% retention in 45 minutes On Oct 26, 1959, the heterophil antibody was absent from the blood The white blood cell count was 6,000 per cubic millimeter, with a differential count of 68% segmented neutrophils, 2% nonsegmented neutrophils, 21% lymphocytes, 5% monocytes, 3% eosinophils, and 1% basophils

The patient has remained well, with no evident residuum of his infectious mononucleosis There is no sign of testicular atrophy, and his sexual function apparently is normal (He has consistently refused both testicular biopsy and procurement of a specimen of semen)

Comment

This man presented a classic clinical and laboratory picture of infectious mononucleosis He also had liver involvement, manifested by an enlarged tender organ, bilirubinemia, and test results compatible with parenchymal disease (elevated transaminase values, positive flocculation, and slightly elevated alkaline phosphatase levels) There was also a complication, to our knowledge never before reported, namely, testicular involvement This man had noted the gradual onset, about 10 days after becoming ill, of pain in both testes Thereafter, both glands had swollen to about three times their normal size and were exquisitely tender With no more than symptomatic therapy, a fairly rapid regression of the testicular signs and symptoms began about two weeks after onset Six weeks after the appearance of his first symptoms the patient was clinically ready for discharge from the hospital and has remained well to the time of writing without apparent residual malfunction

Summary

A 29-year-old man, whose case is described, had infectious mononucleosis His clinical course was complicated by both hepatitis and orchitis, the latter to our knowledge not having been reported previously

221 S 4th St (Dr Ralston)

CARDIAC ARREST DUE TO VENTRICULAR HERNIATION

REPORT OF A CASE OF TWO SUCCESSFUL CARDIAC RESUSCITATIONS

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and
Fay S Anderson, M D., Los Angeles

During the past few years cardiac resuscitation has become a well-established procedure Because the time factor is the most important single element, the percentage of successful revivals has been much higher inside the operating theater than outside Both cardiac catastrophies to be presented below occurred outside the operating room Favorable circumstances which permitted immediate treatment made resuscitation of the patient possible each time

Unless effective cardiac action is immediately restored, there are three reasons why it is usually advisable to open the pericardium (1) proper inspection of the cardiac muscle may be difficult or impossible through the pericardial layer, (2) rhythmical compression of the heart sufficiently strong to maintain a desirable arterial pressure and circulation can rarely be performed with the pericardium intact (3) any traumatic insult to the heart may produce considerable serous or hemorrhagic intrapericardial effusion, which necessitates an opening for drainage to prevent a tamponade A dangerous complication of a pericardiotomy can be myocardial herniation through the incision, particularly if this opening is of medium size To illustrate this danger we are presenting the following case

A [illegible] year-old woman was admitted with a his- [illegible] aving been stabbed with an ice pick in [illegible] anterior part of the chest about one hour [illegible] to admission She was completely irrational [illegible] d in profound shock On the basis of the admission findings, a tentative diagnosis of hemopericardium and cardiac tamponade was made Pericardial aspiration was unsuccessful Conservative measures restored the blood pressure and improved the patient's general condition which remained fairly good for several hours, after which, however, progressive deterioration set in A second pericardiocentesis was attempted After aspiration of about 50 cc of blood, severe arrhythmias appeared on the oscillographic monitor, and seconds later all electrical activity ceased No apical heart beat was audible Within 60 seconds a thoracotomy was performed, the pericardium was opened and about 700 cc of dark clotted blood removed For a period of three minutes, until anesthetic assistance arrived and oxygen ventilation could be instituted mouth-to-mouth ventilation was carried out Cardiac activity returned spontaneously as soon as the heart had been decompressed [illegible] 2-mm perforation of the right ventricle at the anterior superior margin was sutured and the pericardium then partially closed, leaving a 3-cm opening for drainage Light general anesthesia was required for closure of the chest

At the conclusion of the procedure the patient was alert and vital signs were stable Digitalization was begun, and the patient was transferred to the postanesthesia recovery room The achieved improvement, however, did not last About eight hours after the first cardiac resuscitation, her temperature was 103 6 F (39 8 C) and she was dyspneic with shallow, rapid respiration and a retracting chest The sputum contained blood, and a chest x-ray revealed marked pulmonary congestion Attempted left thoracentesis yielded only 30 cc of serosanguinous fluid Surface cooling measures were instituted, and chlorpromazine was administered to control shivering The patient's condition remained reasonably stable but no progress was seen Instead, periods of disorientation, lethargy, and hypotension began to occur on the second postoperative day

About 62 hours after her first cardiac arrest, the patient suddenly became apprehensive and dyspneic, and then lethargic Within minutes the respiratory pattern changed, resulting in shallow, inadequate exchange Emergency tracheotomy and application of positive pressure to assist respiration briefly improved the situation, but were followed by disappearance of both peripheral pulse and apical heart sounds the diagnosis of cardiac standstill was made for the second time In view of the possibility of either postoperative fusion of the opening in the pericardium with subsequent recurrent tamponade or herniation of the ventricle through this opening the chest was opened without delay Thoracotomy through the previous incision revealed an edematous and thickened pericardium, with the left ventricle herniated through the drainage opening from the previous resuscitation The heart was in asystole Complete reopening of the pericardium rhythmical compression of the heart, and intracardiac injection of calcium chloride and epinephrine restored cardiac action The pericardium was left completely open and the patient began to react while the chest was being closed

Except for a brief period of severe hypotension and fever about two hours after the second resuscitation controlled by cooling measures and institution of intermittent positive pressure, the patient's condition steadily improved and she was discharged to her home two weeks later A follow-up

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From the dep[illegible]ts of surgery and anesth[illegible], Los Angeles County General H[illegible] University of Southern [illegible]a School of Medicine, and Coll[illegible]edical Evangelists

over 10 months revealed no cardiovascular or mental sequelae

Summary and Conclusions

Two cardiac arrests in the same patient, presented above, occurred both outside the operating room The first one was due to cardiac tamponade and the second to herniation of the ventricle through the pericardiotomy opening

Both respiration and circulation can be maintained artificially by primitive measures for a short period An opening of medium size for drainage of the pericardium may lead to herniation of parts of the heart, the pericardial incision cannot be too large

Successful resuscitation was possible in each instance because, when the catastrophies occurred, two physicians trained in the technique of cardiac resuscitation were present, and the necessary equipment for completing the resuscitation was available

1200 N State St (33) (Dr J S Denson)

SUBDURAL HEMORRHAGE

Charles D Aring, M D, Cincinnati

Subdural hematoma is an adversary apt to lull the physician into a diagnosis that becomes a death warrant It is a relievable condition when it is recognized promptly There is justification, therefore, in repeatedly calling its multifarious syndromes to the attention of physicians

In subdural hemorrhage, blood accumulates beneath the dura, the source of the bleeding almost always is venous Many thin-walled veins bridge the space between brain and the dura, and the force that sheers one or more of them can be relatively minor if it is delivered under proper conditions and in the right direction In not a few cases, a blow of analogous force has been experienced many times previously without trouble If the patient is suffering from a blood dyscrasia or is receiving anticoagulants, it is thought that there need be no trauma to produce subdural bleeding, it may then occur in the ordinary course of events In many cases the offending bump is readily forgotten, or it may not be recalled (because of mental malfunction) until some time after the subdural hemorrhage has been evacuated Skull fracture is infrequent in subdural hemorrhage, having been found in but 14% of cases coming to autopsy[1]

Since the source of hemorrhage is a small vein, the accumulation of blood is slow, and some time (hours or days) may elapse between the blow and the symptoms At times months pass before the correct diagnosis is made Too often a fresh or a chronic subdural hemorrhage turns up unexpectedly at autopsy In children the rare calcification of the subdural hemorrhage testifies to the organism's ability to survive with it

In patients brought to general hospitals, many without history, the diagnosis is made most often by keeping in mind three cardinal manifestations beside the usual signs of a stroke Next in importance to a high titer of suspicion for the condition are (1) headache, (2) mental signs and (3) changing levels of consciousness

There is absolutely no diagnostic substitute for a high titer of suspicion for the condition, physicians dealing with 'general hospital material" must give every case of brain disease one clear, cool moment of thought before venturing to dismiss the possibility of subdural hemorrhage It does not matter if a story of trauma is missing, although bruising or abrasion of any part of the anatomy is some substitute for it, these too may be missing With the best will, there are some one-half dozen patients with unsuspected cases yearly reaching the pathologist in an 850-bed general hospital with an autopsy percentage of 63

Subdural hemorrhage is termed the great neurological imitator because it is so often misdiagnosed At one time or another it has been called almost every known disease affecting the brain Perhaps the most frequent confusion is with strokes of various types, it has masqueraded as one or another of the infinite variety of mental diseases as encephalitis, brain tumor, epilepsy, and cerebral arteriosclerosis There is hardly a category of brain disease whose manifestations have not in some degree been imitated by subdural hematoma Subdural hemorrhage is found in the youngest of infants, where it lurks under the guise of drowsiness and feeding problems and in people hoary with age, when it is most frequently misdiagnosed as a stroke

It is not known why cerebral decompensation occurs when it does in patients with subdural hematoma But once this process begins, usually with deep coma and a dilated pupil on one side, the prognosis is poor It seems that this condition is due to interference with the blood supply to the midbrain or more likely with the venous outflow from it Subdural hematoma should be evacuated before this cerebral decompensation sets in, and since no one can predict when it will occur, there should be no delay in treatment once the diagnosis is made Some patients appear to resist this partial decerebration and harbor their subdural hematomas in a potentially curable state for prolonged periods—for

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From the Department of Neurology University of Cincinnati College of Medicine and the Cincinnati General Hospital months, years, or the remainder of their lives (chronic subdural hematoma) Needless to say, their function is severely handicapped by reason thereof

In a study done in 1940[2] in the state hospitals of Massachusetts, 245 cases of subdural hemorrhage were found among 3100 consecutive autopsies on mental patients, an incidence of 7 9% This seemed to indicate that people were being committed to state hospitals harboring a subdural hemorrhage or that undetected accidents may have occurred in these institutions

The cerebrospinal fluid may be normal if the injury of the head that resulted in the subdural accumulation of blood was minor or occurred months previous Displacement of a calcified pineal gland in the roentgenographic study of the skull may be helpful in diagnosis, however, if subdural hemorrhage be bilateral, as it is not infrequently, the pineal gland may not be displaced

When the diagnosis of subdural hemorrhage cannot be excluded, bilateral trephine exploration of the parietal-temporal region should be carried out or a carotid angiogram performed, whichever is the most realistic to the medical talent and equipment at hand Since burr-hole trephination done under aseptic conditions is a minor surgical procedure, it ought to be done rather more than less often This is in accord with the neurological tenet to strive to make a diagnosis of a relievable lesion, rather than resting content with a diagnosis that sentences the patient to permanent invalidism or death

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IOPHENOXIC ACID AND SERUM-BOUND IODINE VALUES

Robert Shapiro, M D
and
Evelyn B Man, Ph D, New Haven, Conn

In 1957, Astwood[1] reported on a patient with hyperthyroidism whose serum-bound iodine level was 4,200 mcg per 100 ml A single dose of radioactive iodine led to a clinical remission of the hyperthyroid state but the bound iodine level in the serum remained astronomically elevated Within a short period of time, a number of other patients presented themselves with serum-bound iodine values of 2,000 to 14,000 mcg per 100 ml in the face of normal or increased radioactive iodine uptake and normal urinary iodine excretion Of the 15 patients studied, 9 admitted previous exposure to iodine in one form or another There remained, however, six patients who were unaware of any exposure to iodine, including radiopaque, diagnostic studies

An exhaustive chemical and spectroscopic analysis of the serum of the first patient finally led to the isolation of a compound which had the chemical formula of iophenoxic acid (Teridax) A meticulous search and exhaustive inquiry of neighboring hospitals and radiologists revealed that these six patients had undergone cholecystographic examination without their knowledge In each instance, the cholecystographic medium used was iophenoxic acid From a semilogarithmic plot of the protein-bound iodine level against the time interval after ingestion of iophenoxic acid, Astwood calculated that it would take 33 years for the protein-bound iodine level to return to that of 1 mcg per 100 ml after a single dose of iophenoxic acid Astwood's data have been amply confirmed by one of us (E B M)

Recently, two 4-day-old infants were seen with serum-bound iodine values of about 4,000 mcg per 100 ml In each instance, the mother had received iophenoxic acid for cholecystography about two years prior to delivery At the time of this writing this problem is under further study, but it would appear from these preliminary determinations that iophenoxic acid is able to cross the placental barrier into the fetal blood stream some years after its ingestion by the mother

Because of these facts, it seems logical to abandon the use of iophenoxic acid since it completely invalidates one of the most accurate methods for studying thyroid function This is particularly appropriate in view of the presence of other equally satisfactory or superior radiopaque contrast media which do not elevate the serum-bound iodine level so greatly for such a long period of time After iopanoic acid (Telepaque) is administered, the butanol extractable iodine level returns to normal in most patients by 12 weeks, in a small series of normal subjects who took bunamiodyl (Orabilex), the butanol extractable iodine level was normal within 4 weeks[2]

1450 Chapel St (Dr Shapiro)

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From the Department of Radiology, the Hospital of St Raphael, and the Departments of Radiology and Internal Medicine, Yale University School of Medicine

COMMITTEE ON COSMETICS

Report to the Committee

The Committee on Cosmetics has authorized publication of the following report
Veronica Lucey Conley, Ph D , *Secretary*

PHOTOBIOLOGICAL RESEARCH WITH PARTICULAR REFERENCE TO SKIN

Harold F Blum, Ph D , Princeton, N J

There are many biological effects of light, which pose a variety of problems and entail a variety of methods of approach, however, there are certain common principles involved in all This discussion is confined largely to the effects of sunlight on the skin

Wave-length Variable

Apart from certain rare diseases (in which other parts of the spectrum are concerned) and experimental use of extraneous photosensitizers, the principal effects of sunlight on human skin are produced by wave lengths shorter than about 0 32 μ (0 32 μ = 320 mμ = 3,200 A) There are certain important diseases of the skin in domestic animals that are produced by other wave lengths, but, for physiological or dietary reasons, these do not have their counterpart in human skin [1] Wave lengths shorter than 0 32 μ, which comprise only a tiny fraction of sunlight (i e 0 01%), produce the various responses of sunburn, antirachitic action, and cutaneous cancer Evidence of the latter partly stems from the fact that one can produce skin cancers in 100% of experimental animals by repeated doses of these wavelengths [2]

Whereas sunburn and production of cancer may possibly involve basically the same photochemical process, antirachitic action certainly involves a quite different one The reason that all have the same long-range wave-length limit at 0 32 μ may be regarded in a way as "accidental," since different chromophores are involved We apply the term chromophore to the substance whose molecules capture the quanta of radiant energy necessary to forward the photochemical reaction basic to the particular photobiological response

Classification of Photobiological Responses

One fundamental way of classifying photobiological responses might be according to their chromophores In any case, knowledge of the nature of the chromophore is desirable concerning any of these processes we study There is a useful method for determining the chromophore which works well in some cases but is not without its difficulties concerning both measurement and interpretation This method consists of comparing the action spectrum with the absorption spectrums of substances suspected of acting as the chromophore Absorption spectrums are maps of the amount of absorption of light in terms of the wave length, they are, of course, characteristic of the specific chemical substances concerned An action spectrum is a map of the effectiveness of various wave lengths in producing a given photobiological effect, it may be determined in a variety of ways according to the system being studied In other publications I have discussed some of the sources of error in such measurements [3]

Relationship of Action and Absorption Spectra

Under ideal conditions, the action spectrum may be expected to agree with the absorption spectrum of the chromophore In figure 1A, action spectra for antirachitic action, measured in rats by two independent investigators, are compared with the absorption spectrum of 7-dehydrocholesterol, a precursor of vitamin D The agreement is obviously not perfect, it might look somewhat better or worse according to the way the data are plotted Thus, more evidence is needed to support the idea that a sterol of this type is the chromophore We know that, in vitro, ultraviolet light can bring about chemical change that converts such precursors into vitamin D, after all the evidence is taken into account, there is little doubt that this same reaction goes on in the skin or on its surface The point I would like to emphasize is that the action spectrum alone does not provide enough evidence in this case

In cases of sunburn, the action spectrum, commonly called the erythemal spectrum, does not agree well with the absorption spectrum of any substance suspected as being the chromophore

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Presented at the Fifth Symposium of the Committee on Cosmetics at the Clinical Meeting of the American Medical Association in Dallas Texas Dec 2 1959

Figure 1C shows the familiar erythemal spectrum, plotted in such a way that it may be compared with absorption spectra for protein and nucleic acid, which are under particular suspicion as the chromophore In this case, the discrepancy is not difficult to explain away although, in doing so, we do not identify the chromophore The optics of the skin are complex, and one has to oversimplify greatly or abandon any attempt at analysis of the situation

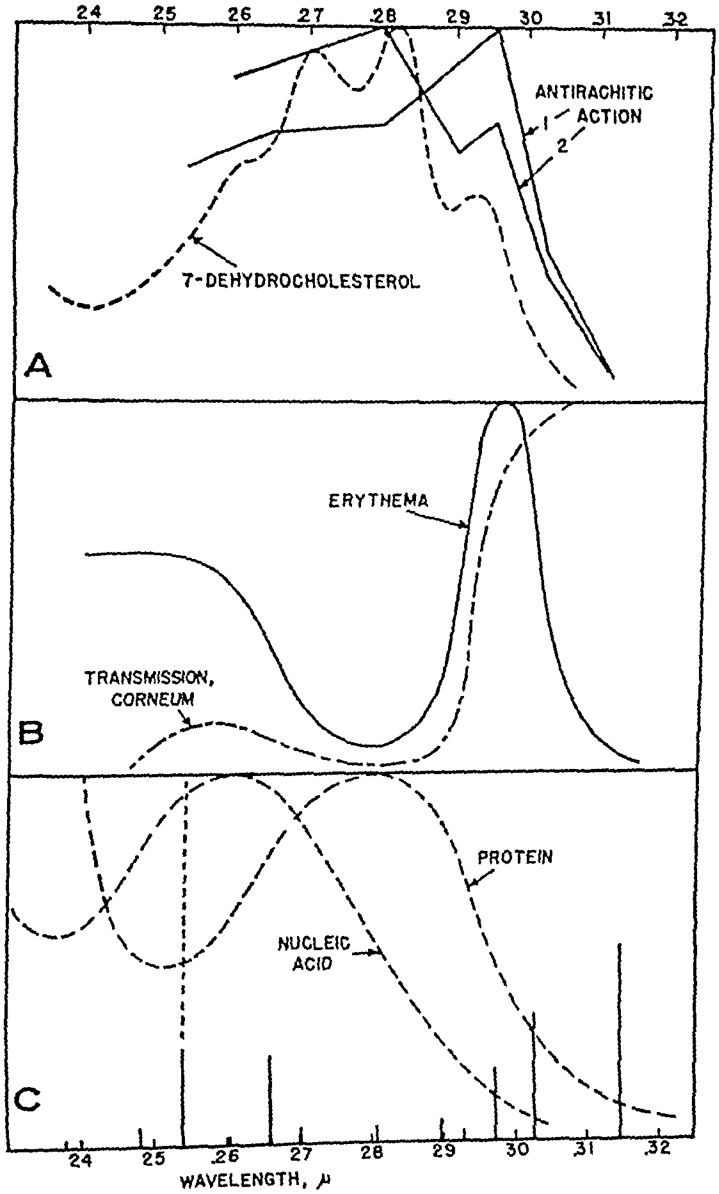

Fig 1 —*A*, comparison of action spectra for antirachitic action on the rat and absorption spectrum of 7-dehydrocholesterol (line 1, according to Bunker and Harris[17], line 2, according to Knudson and Benford[18]) *B*, erythemal spectrum for human skin, spectral transmission of a sample of human corneum (according to Lucas[19]) *C*, absorption spectrum of nucleic acid and protein, with mercury arc emission Solid lines represent emission of intermediate pressure mercury arc, emission from low pressure mercury arc is chiefly at 0 2537 μ as indicated by the broken line

For the purpose, one may assume that the epidermis is made up of only two layers (1) the dead corneum and (2) the underlying layer of living cells (the Malpighian layer)—beneath this, in the dermis, lie the most superficial blood vessels It is known from direct measurements that, in human skin, a small amount of the incident ultraviolet radiation penetrates below the epidermis, an amount negligible in most cases[4] The erythema represents the dilation of the minute vessels just beneath the epidermis, and it seems most reasonable to think that the photochemical reaction responsible for this vascular dilation takes place almost entirely in the epidermis, presumably by the production of some dilator substance there which diffuses down to the minute vessels in the dermis If we assume that the layer of living cells is the locus of the photochemical reaction and that the corneum, which lies superficially, only acts to filter out some of the incident ultraviolet light, we can explain the shape of the erythemal spectrum in a qualitative or semiquantitative way The corneum is an excellent filter for the wave lengths concerned, since it is composed largely of protein, which absorbs strongly in this spectral region, although the absorption is apparently greatly enhanced by scattering of the radiation due to the flakes and particles of which the corneum is composed

In figure 1*B*, note that protein absorption by the corneum and the minimum of the erythemal spectrum occur at nearly the same wave-length We can thus reason that the minimum in the latter reflects the filtering action of the corneum to a greater extent than it reflects the absorption spectrum of the chromophore, whatever the latter may be The whole matter is complicated by recent evidence that photochemical reaction in the corneum *itself may* contribute to the vascular dilatation[5] Thus, the action spectrum for erythema might prove to be quite complex, even if it could be measured directly In any case, however, absorption in the corneum greatly alters the erythemal spectrum that we are able to measure, and, hence, this cannot give an accurate picture of the absorption spectrum of the chromophore or chromophores Discussion of other complicating factors may be found in the literature[4]

One may wonder why the action spectrum for antirachitic action does not also show a minimum of absorption at 0 28 μ The answer is not difficult—since, in the rat, (the animal used in these experiments) transformation of the precursor to vitamin D takes place superficially in the corneum or on its surface[6]

We are left with something of a puzzle regarding the action of light on the cells of the Malpighian layer of the epidermis Action spectrum studies, as well as other evidence, indicate that the locus of the lethal action of ultraviolet light on viruses and on micro-organisms is in the nucleic acid moiety With the recent general interest in nucleic acids, it is, perhaps, not surprising that the idea has become rather widespread that these substances are the chromophores for all effects of ultraviolet light on cells As illustrated in figure 1*B*, if we take into account the filtering action of the corneum, we might well suspect nucleic acid as being the chromophore for the reaction underlying sunburn It needs to be remembered, however, that there are many substances in cells besides nucleic acid, it is possible that some of these may well act as chromophores in some cases Indeed, we know that ultraviolet light causes changes in permeability of mammalian red blood cells, which contain virtually no nucleic acid[7] In the latter case, one thinks of protein as the most likely chromophore, although there is reason to suspect the lipid fraction too Protein could well be the chromophore for the erythemal process insofar as the erythemal spectrum can tell us (see fig 1) There is still room to suspect other substances with wave-length limits of absorption at about 0 32 μ

Use of Monochromatic and Polychromatic Light

Clearly, one cannot obtain a reliable action spectrum without using monochromatic light We mean, by this term, light restricted to a narrow band of wave lengths, since some compromise always has to be made regarding spectral purity To work with monochromatic light over the necessary wave-length range at sufficiently high intensities requires considerable equipment and care In some cases, it is not feasible to use monochromatic light in photobiological studies, but there are many studies that can be carried out with polychromatic light, i e, with a mixture of wave lengths Indeed, there are times when studies with polychromatic light may yield information that would be missed by using monochromatic light exclusively So it is rather troublesome to find the idea current that photobiological studies made with other than monochromatic light are inexact or deficient It is often assumed that "pure' effects are studied with monochromatic light, whereas 'mixed' effects are necessarily studied with polychromatic light This is not true The use of monochromatic light in no way assures purity of effect For example, many studies have been made in which radiation was used from a low-pressure mercury arc, in an appropriate envelope, a high proportion of which consists of wave length 0 2537 μ This wave length falls near the maximum of absorption of nucleic acid, but this by no means ensures that this radiation affects only that chromophore (fig 1C) It is clear that one cannot expose a living cell to this wave length without having a certain proportion of the energy absorbed by protein As a matter of fact, some of it must be absorbed by many other substances in various parts of the cell This does not mean that all the light absorbed in the cell produces photochemical reaction, but it is quite certain that some of it acts through chromophores other than nucleic acid Some of the resultant effects may be negligible or relatively unimportant, others may not come to our attention because we focus on only one aspect of the cell response For example, when we produce lethal effects with this wave length in micro-organisms, which seem clearly to have nucleic acid as the chromophore, we are almost certainly altering the permeability of membranes at the same time, possibly through action on the proteins but pretty clearly not by direct action on nucleic acid The effect of permeability may or may not be negligible in this particular instance, but, in any case, the usual methods of study do not bring it into evidence

The absorption spectra of complex molecules such as those which act as chromophores in these photobiological responses do not have sharp spectral limits but taper off gradually This is correspondingly true for the action spectra, as may be seen in the erythemal spectrum (fig 1*B*), where it is clear that no exact, long-wave length limit can be assigned It may be of interest to examine this particular case, where several studies have been made using the mercury arc as the source of ultraviolet radiation The emission of mercury is a series of discrete spectral "lines," separable with a monochromator, the positions of which are indicated in figure 1*C* The intensities and widths of these lines may vary with the conditions, but their spectral positions do not change For example, by reducing the pressure, most of the energy may be concentrated in the 0 2537 μ line, the others remaining, however, as traces In studying the erythemal spectrum, several workers have found a slight response to the 0 313 μ line but none to the next longer line at 0 322 μ So one may say that the measurable limit lies somewhere between these two wave lengths, at about 0 32 μ It might be better to say that this is the feasible, measurable limit, since it is, in part, determined by the intensities of radiation that can be used If it were feasible to employ more intense radiation (which might be done effectually by sacrificing spectral purity), it should be possible to elicit a response with longer wave-lengths Correspondingly, persons with unusually high sensitivity might be expected to respond to moderate intensities of somewhat longer wave-lengths than 0 32 μ

A case in point involves some measurements made on patients with urticaria solaris In some cases of this disorder, the patient responds to wave-lengths in the blue and violet portion of the spectrum, specifically between about 0 4 μ and 0 5 μ, with a wheal confined to the exposed area Several of these cases have been described in the literature, two of which I have studied[8] In 1945, Baer, Sulzberger, and I[9] studied another patient with urticaria solaris, using an intense mercury arc with filters to restrict the wave lengths This time a characteristic wheal was obtained with wave lengths in the erythemal range and, also, with high dosage with the 0 365 μ line, to which normal skin does not respond Although the wheal was indistinguishable from that of patients responding to wave lengths 0.4 μ to 0.5 μ, it was clear that the chromophore, and, hence, the etiology, was different. Two types of urticaria solaris could thus be differentiated: one responding to wave lengths in the blue and violet (urticaria solaris λ 4,000 A to 5,000 A) and one responding to ultraviolet light shorter than 0.37 μ (urticaria λ >3,700 A). A few months after studying the patient of Baer and Sulzberger, I saw another patient who was one of two being studied by Beal. He used a monochromator and filters with a mercury arc. Beal[10] elicited responses with wave lengths up to 0.334 μ, but apparently not with 0.365 μ. It seems likely that, in these cases, the etiology was the same as that we described as sensitive to wave lengths shorter than 0.37 μ and that the chromophore may well be the same as the chromophore in normal erythema, in spite of the differences in the measurable long-wave-length limit which may be credited to the difference in the intensity of the radiation used for testing and/or differences in the sensitivity of the patients. It is of course possible that another chromophore is involved, but this would be difficult to establish. In view of the uncertainties of measurement in these cases one cannot split hairs—or wave-lengths.

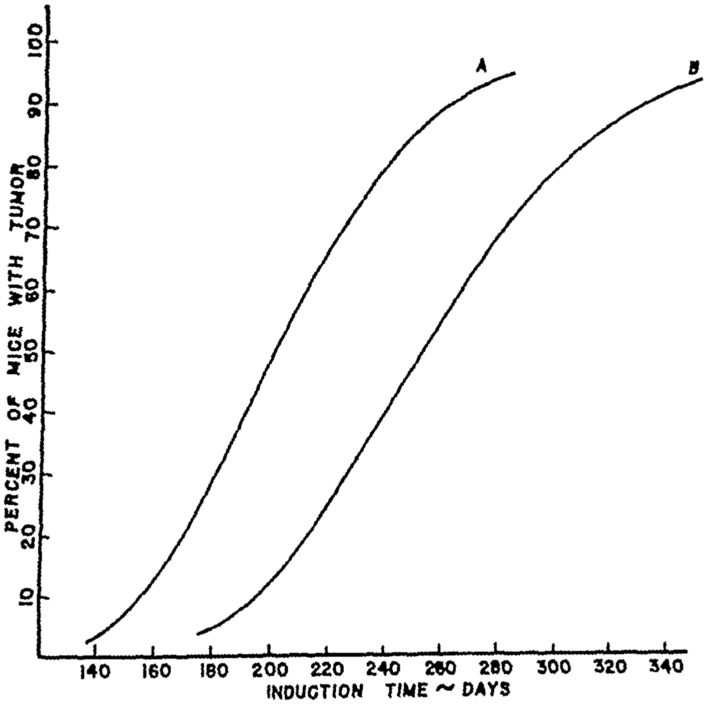

Fig. 2.—Limits of accuracy in comparison of groups of mice subjected to repeated doses of ultraviolet light. Curves A and B represent expected range of time to appearance of cancers if experiment were repeated 20 times under the same conditions with 10 mice per experimental group (according to Blum, Grady, and Kirby-Smith[15])

There seems to be an unfortunate misconception regarding the long-wave-length limit of carcinogenesis, which probably stems from a misquotation or misinterpretation. Independent studies by several workers all indicate that the long-wave-length limit for cancer induction in mice and rats is at about 0.32 μ. This evidence was reviewed in another report.[11]

Experimental Animal Studies

I want now to mention briefly some recent studies in my laboratory. In these studies, the ears of albino mice were exposed to single doses of ultraviolet light.[12] After the irradiation, there are changes in the ear of the mouse corresponding to those seen in sunburn of human skin, without the tanning, of course. Perhaps the most interesting aspect is hyperplasia of the epidermis, which may be followed quantitatively by counts of mitotic figures. The mitotic count rises for a few days and then falls off gradually toward normal. Soffen[13] has recently extended these counts, and, by making appropriate corrections, it is possible to arrive at certain conclusions, although a complete quantitative interpretation has not been achieved. Among other things, the rapid increase in mitotic counts is accounted for by rapid proliferation of only a few clones. During the phase of rapid division, the cells of these clones divide as often as once a day. It is interesting to compare this rate with that of induced cancers in the same strain of mice subjected to repeated doses of ultraviolet radiation. The latter has been estimated by measurement of the relative growth rate of those tumors.[14] The "average" growth rate corresponded to cell division every six days, although the comparison cannot be drawn too closely because, for the most part, the tumors were not of the epidermal type. *The point of interest, however, is that we see once again that rapid proliferation of cells is not in itself diagnostic of cancer. The great difference between rapid growth in cancers and in normal tissues is that, in the cancer, the rapid rate of cell proliferation is inherited by the cells, whereas in normal cells it is not.*[2] The curves in figure 2 show that, in spite of the high rates of cell division in the epidermis after a single dose of radiation, the tissue virtually returns to the normal state within a relatively short time, cancers do not appear in these mice after single doses of this radiation.

In the field of carcinogenesis by ultraviolet light, good quantitative data have been obtained by studies on a large number of mice. I have discussed these experiments and their implications elsewhere at length[2] and can only mention here a feature of particular importance regarding the method. It was possible by repeated dosage to induce cancers of the skin of the ears in up to 100% of mice, it was found that the distribution of the time from onset of experiment to appearance of the cancers followed a clean statistical distribution on which the curves in figure 2 are based. This permits close evaluation of the reliability of experiments of this type.[15] Let us assume, for example, that the same experiment was repeated 20 times under exactly the some conditions and that 10 animals were used in each experiment. The results would be expected to vary to a certain extent due to chance factors, even though the experimental treatment was the same Figure 2 illustrates the extent of this expected variation, the two curves represent the range of difference to be expected within the 20 experiments Obviously, if only two experiments were performed, there would be a risk of 1 20 of this much variation between the two If the two experiments are compared, with 10 animals used in each experiment and with some given factor varied, it could not be stated with confidence that the result was different unless the two curves differed more than do those in the figure For the particular conditions represented, the respective times at which 50% of the mice developed tumors would have to differ by several weeks between the two groups, if they were to be considered significantly different The situation could be improved by increasing the number of animals, since this would decrease the expected difference between the two curves On the other hand, the reliability of results could be greatly decreased by a high mortality among the animals in the course of the experiments If a comparison is made, in terms of the percentage of animals with tumor at some given time (which is all too common practice), the apparent result could be very different according to the time chosen for comparison (lines A and B in fig 2) Hence, such an estimate could be wholly unreliable Thus, it is clear that one must be skeptical of his conclusions, unless the experiments are carefully examined statistically In describing experiments, it is desirable to state clearly the conditions of the experiment, the number of animals used and the number of those surviving, the methods of comparison, and the statistical distribution Otherwise, the reader has no way of estimating the reliability of the experiments or the seriousness of the conclusions that have been drawn At this point, the experimenter may well ask the aid of a statistician, but the experimenter must not expect much useful advice unless he can provide enough data and precisely state the conditions under which these have been obtained

Even when the researcher is confident that the results are statistically significant, there is still, of course, the problem of interpreting them In experimentally produced cancer, when a given factor produces statistically significant differences, there is still the question of how the particular factor has operated, this may not be easy to answer satisfactorily[16]

Comment

I think I may now close with a general statement to the effect that photobiological action on skin is susceptible to quantitative study that may reveal a good deal about the underlying processes and, perhaps, information of more general interest But one needs to proceed carefully, with due respect for the tool he is using and caution in his interpretations Above all, may I make a plea for more complete quantitative studies, since it seems clear that, even in the brief material I have presented, there are instances where qualitative or semiquantitative studies might have led to erroneous conclusions And let me emphasize that by quantitative studies I mean not only quantitative measurements but quantitative thinking about them

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THE ADRENOGENITAL SYNDROME

THE adrenogenital syndrome due to congenital adrenocortical hyperplasia is another example of an inborn error of metabolism in man, which has enjoyed closer scrutiny and etiological clarification in recent years This condition is hereditary and behaves as a Mendelian recessive characteristic Its imprint is heavier on female children, in whom it produces masculinization of the external genitalia owing to the initiation of the disorder during fetal life This disease constitutes one of the commonest causes of female pseudohermaphroditism

The incrimination of the adrenal cortex in this syndrome has long been a matter of morphologic record—in patients who died, this gland was many times normal size Since the availability of the Zimmermann reaction for the measurement of urinary 17-ketosteroids, it has repeatedly been shown that the androgens (of adrenal origin) are regularly elevated in patients with this condition In recent years, the administration of hydrocortisone or its many analogs has been reported to suppress the urinary 17-ketosteroid levels and bring about a clinical remission as well[1]

Hydrocortisone is the "key" adrenocortical hormonal secretory product In the face of inadequate secretion of this substance, more pituitary adrenocorticotropin is released, leading to an enlargement of the target gland Hechter and Pincus[2] have uncovered the major final steps in the biosynthesis of hydrocortisone by perfusion of the beef adrenal gland This involves a series of hydroxylations of the steroid skeleton, each step controlled by a specific enzyme In part, this sequence is as follows

$$\text{progesterone} \xrightarrow{1} \text{17-hydroxyprogesterone} \xrightarrow{2} \text{17-hydroxycorticosterone} \xrightarrow{3} \text{hydrocortisone}$$

Bongiovanni and Eberlein[3] have shown that pregnanetriol (a urinary product of 17-hydroxyprogesterone) is regularly excreted in large amounts by patients with the adrenogenital syndrome They suggested that a block at (2) was thereby demonstrated Direct enzymatic study of adrenal tissue has substantiated this view[4] A consequence of the deficient production of hydrocortisone is the secretion of large amounts of androgens (representing intermediary metabolites or other end-products) during an attempt to overcome the defect, hence the virilizing manifestations The provision of hydrocortisone, in modest replacement doses, relieves the chemical dilemma Later, these same workers[5] revealed a second type of defect in this syndrome, wherein the interference with the pathway occurred at (3) Under these circumstances, androgens are produced in large amounts for the reasons described, but in addition there is likely to be hypertension, since a defect at this point also leads to the overproduction of desoxycorticosterone, a well known salt-retainer In the latter variety, 11-hydroxylation is at fault and a portion of the steroidal precursors which are normally not converted into 17-hydroxyprogesterone follow a slightly different course toward corticosterone (compound B) In the absence of 11-hydroxylation, the desoxycorticosterone cannot be converted into corticosterone

There is a third form of this virilizing disorder accompanied by extreme loss of sodium and water, with death in the early days of life unless the condition is quickly recognized and rigorously treated. To date no basic biochemical difference in this variety has been recognized Some workers have suggested a more severe form of the first type, as evidenced by the excretion of very large amounts of pregnanetriol and the lesser quantities of hydrocortisone apparently secreted in this form[3] From time to time, it has been proposed that a hormone with active "salt-secreting" properties occurs in this type, but complete substantiation of such a view has not been forthcoming Further investigation may reveal a defect differing from those described above

An additional facet of these studies deserving mention deals with the severity of the disorder All too often the "all-or-none" concept abides with us in considering human disease Because the deficient production of hydrocortisone is recognized as the basic biochemical defect in the adrenogenital syndrome, although the precise site may vary, it at first might have appeared that affected persons would reveal an absence of this critical hormone Under such an assumption, patients with this syndrome should manifest the alarming symptoms of complete adrenocortical insufficiency This has not been the case Closer study has indicated that there are all degrees of interference with the biosynthesis of hydrocortisone and that in most cases, with greater biochemical effort, under the stimulation of large amounts of adrenocorticotropin, the adrenal cortex may compensate fully Nonetheless, the consequences of such compensation, i e, adrenocortical enlargement and the production of androgens, produce the unwanted virilization Appropriate therapy with hydrocortisone, or suitable analogs, throughout life represents one of the truly specific applications of this drug to human disease

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EARLY YEARS OF THE LANCET

The initial period following the founding and establishment of the *Lancet*, almost 150 years ago, provides evidence for an interesting document in medical journalism Thomas Wakley, founder and editor for more than 40 years, was not trained in journalism, he was not even recognized as a brilliant student of English composition during his liberal arts training He finished his formal medical education at the age of 22 and qualified as a Diplomate of the Royal College of Surgeons Thereupon he began a country practice, not far from the village of his birth He pursued this only a few months and then returned to London where medical competition was acute The hours that were not spent in practice were dedicated to the preparation, possibly not fully recognized at the time, for a career in medical journalism He found time each day to read good books and to write for the love of writing These hours helped him establish a firm footing in literature and developed his talents in literary skill The combination of medical practice and a deep interest in literature were his two assets basic to the editorship of the *Lancet*

The first issue appeared on October 5, 1823 The dissemination of medical information was his primary purpose However, the task of fighting the opponents of progress in medicine was so sensational that it attracted as much attention as his plans for the improvement of postgraduate medical education, for the practitioners outside of the large medical centers Editorials were published in the early issue of the *Lancet* 'that would not have appeared had the editor been a man of wider experience, but the harm that they did was small—and the value of his fearless ardour to the cause of reform was incalculable"

Some of the richest sources of original communications were lectures delivered by distinguished surgeons and physicians of the day to medical students, for a fee The address by Sir Astley Cooper, Surgeon-Sergeant to the King, appeared in the first issue Many teachers resented the broad, professional dissemination of their lectures—'their trade secrets'—and denounced Wakley as a literary pirate and a dispenser of moral garbage He remained firm, however, in his belief and practice that the teaching of the professors in the medical schools was common property for other physicians and for medical students By his own words Sir Astley Cooper stood almost alone in permitting publication of his school lectures in the *Lancet* "although publication of my lectures exposes me to the critical ordeal of my professional brethren, yet I fear it not, I care not who may be made acquainted with the doctrines I advance, the instructions I give, the principles I inculcate, while in this theatre Therefore I am perfectly indifferent as to who publishes them, and equally indifferent as to who may be made acquainted with them"

Mr Abernathy, senior surgeon at St Bartholomew s Hospital, and second only to Cooper in medical fame, was not convinced that his lectures should be free for publication In fact, he took his case to court and caused Wakley to write as follows "He may possibly have vanity enough to suppose that we shall reprint his lectures On this point his mind may be perfectly at ease, our pages have been already obscured with his hypothetical nonsense during six tedious months, and when we read the proof of the last paragraph we felt relieved of a most intolerable incubus" Is it any wonder that Wakley was called "The Battling Editor"

The above occurred before 1825 At the end of the third year of publication the *Lancet* enjoyed a circulation of more than 4,000, which is excellent for a new journal in a land with less than 1,500 physicians Sections entitled, "Chess Table," "Dramatic Lancet," and "Table Talk" were maintained for a few months only and were discontinued to allow for the publication of more scientific communications A similar path has been followed recently by the *J A M A* in regard to the "Leisure Corner" and 'Medicine at Work' The exclusion from the columns of the *Lancet* of all but strictly medical matter "was related to certain idiosyncrasies of the editor" It is trite but true that medical editors have idiosyncrasies in common

Strife between the editor of the *Lancet* and each of three medical periodicals in England at that time brought them almost to the brink of court The *Medical Gazette* was founded in 1827 with the following declaration of war against Wakley "A few years ago a set of literary plunderers broke in on the peace and quiet of our profession Lecturers who had spent their lives in collecting knowledge, arranging it for communication, and acquiring the difficult art of oral instruction, saw the produce of their lives suddenly snatched from them and published for the profit of others, with the additional mortification of finding what they had taken so much pains with, disfigured by bad English and ridiculous and mischievous blunders'

Wakley was not to be outdone He replied, "Some despicable imitations of us have arisen and *stunk*, and become extinguished—one or two are still emitting a *little foetor*

This, and more too, during the early years after the founding of the *Lancet*

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PRACTICABILITY OF ENHANCING SPECIFIC RESISTANCE TO STAPHYLOCOCCIC INFECTION

A symposium and a conference in November, 1957, under the auspices of the American Public Health Association and the American Medical Association focused attention on the epidemiology and ecology of infections due to antibiotic-resistant staphylococci The necessity of more rigorous adherence to established principles of asepsis and antisepsis was stressed, and the establishment in each hospital of an Interdepartmental Committee on Infections was recommended, for continuing surveillance of infection and continuing supervision of procedures directed toward controlling infection This recommendation has been quite generally implemented Moreover, federal, state, and regional health agencies have continued the educational effort, albeit in a somewhat uneven manner A serious effort has been initiated toward cooperation of physicians, health officers, and hospital administrators and personnel on the one hand, and heating and air-conditioning engineers, sanitarians, and architects on the other, in investigating the complex problems of improving sanitation and housekeeping within existing hospitals and improving design and construction of new hospitals Although the record shows how very far these problems are from satisfactory solution, at least a beginning has been made

The A M A conference also stressed the need for more information concerning the pathogenesis and the immune relationships of staphylococcic infection as a basis for supplementation of hygienic measures and therapy by drugs and antibiotics Actually, a considerable reservoir of relevant information exists, and, under the stimulus of the worldwide prevalence of infection by antibiotic-resistant staphylococci, has recently been reviewed systematically Thus "Staphylococcus Pyogenes and Its Relation to Disease," by Professor Stephen D Elek of the University of London, reviews the information contained in some 4,000 references More applicable to the immediate needs of those responsible for guiding the prevention and treatment of staphylococcic infection is a monograph published in French and Italian by Professor D d'Antona of Siena, Italy, which contains about 700 references

The pathogenic staphylococci are, with the possible exception of Streptococcus pyogenes, the most complex, the most versatile, and the most baffling bacteria which afflict man and domestic animals They elaborate a whole battery of toxic metabolites, including free and bound coagulase, several hemolysins, leukocidins, hyaluronidase, fibrinolysin, proteases, lipase, and in some strains enterotoxin Despite all the work done on these metabolites, they have in general not been satisfactorily characterized either in terms of their fundamental biochemistry or in terms of their precise roles in pathogenesis Notable progress in biochemical characterization may be cited in the work of Tager and associates and of Duthie and Haughton on coagulase, and of Woodin on the leukocidin active against human polymorphonuclear leukocytes Recent work by Gladstone and colleagues, by Lack, and by Johanovsky may be cited in relating leukocidin and antileukocidin to clinical infection

In addition to the armamentarium of toxic metabolites, Staph pyogenes has the capacity to invade and persist in tissues and organs The roles of the toxic metabolites, of extracellular materials associated with the bacterial cells, and of the somatic antigens of the bacterial surface in the complex interplay of offensive and defensive action in the body are not fundamentally understood However, the recent work of Cohn and Morse and Rogers and Melly may be cited as evidence that resistance to staphylococcic invasion represents variation on the theme of immunity in all bacterial disease, rather than a law unto itself, as certain investigators have been tempted to assert

Phenomena of allergy also intervene in staphylococcic infections and in procedures of immunization against staphylococci and their products This complex question has been dealt with in detail by d'Antona and by the many clinical and laboratory workers cited by him Johanovsky has also shown that, in experimental animals, hypersensitivity may actually lower resistance to infection

Most pathogenic staphylococci are hosts of lysogenic bacteriophages Possibly associated with this lysogeny, staphylococci possess an extraordinary capacity for adapting to new and adverse environments, notably to the presence of antibiotics Problems of established and emergent antibiotic resistance are too familiar to require emphasis here

The specific and nonspecific constitutional factors of the human host which contribute to infection, healthy carriage, or freedom from staphylococci are in urgent need of elucidation For instance, why are infants, the aged, diabetics, or those suffering from operative trauma more susceptible to colonization and infection from these ubiquitous parasites?

To characterize the components and products of Staph pyogenes on a sound biochemical basis and to elucidate their respective roles in pathogenesis and immunity will unquestionably require decades

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of devoted and costly research Meanwhile, the problem of staphylococcic infection in hospital and community is a present and urgent one in the United States and Canada, the United Kingdom and Western Europe, in the USSR, in Australia and New Zealand, and in Japan and China The areas of the world omitted in the statement indicate lack of adequate documentation known to the writer rather it may be surmised, than lack of staphylococcic infection

If it is not possible at present to discuss the immunobiology of Staph pyogenes var aureus on a satisfactory basis of biochemical analysis, is it possible to consider immunization procedures against staphylococcic infection on the basis of an informed empiricism and clinical experience? As a matter of fact, a very large body of documented clinical evidence does exist A few of the more significant papers reviewed in d Antona's monograph may be cited here These papers record a clinical experience with the therapeutic use of "toxoid" (or as it was originally designated by Ramon, "anatoxine'), which is indeed extensive Thus, Ramon [1] of the Institut Pasteur and his associates in 1946 summarized results with toxoid in over 3,000 cases of staphylococcic infection d'Antona states that 15,000 liters of staphylococcic toxoid produced by the Seroterapeutic and Vaccine Institute at Siena have been given to human subjects in Italy alone A body of experience, numbering many thousands of patients and reported as satisfactory, has been amassed, with the toxoid of the Connaught Laboratories of Toronto It is clear from the methods of preparation employed that the "toxoids" contain bacterial somatic antigens as well as detoxified exotoxins and metabolites Vaccines of intact bacterial cells are, in general, reported as less efficacious

Analysis of the positive values and of the shortcomings of these extensive clinical reports will not be attempted here, nor will the indications, contraindications, and practical details of administration be presented With few exceptions, the clinical observers and their associates in the laboratory have been convinced of benefits obtained in properly chosen cases with judiciously administered toxoid It is profoundly to be hoped that those to whom these reports are relevant will examine the evidence for themselves

There is also literature supporting the use of staphylococcic antitoxin in cases of acute infection with toxemic manifestations [2] More recently, favorable experiences have been recorded with human pooled gamma globulin in acute staphylococcic pneumonia in infants and in patients deficient in gamma globulin [3] Human gamma globulin has been shown in laboratory experiments to synergize well with antibiotics

The immunobiology of Staph pyogenes is in urgent need of thorough investigation both for theoretical and practical reasons Meanwhile, the practicing physician and clinical investigator may find that immunological procedures judiciously applied may offer promise for prevention and therapy in supplementation of other better known procedures

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The complete bibliography will be available on request from the author

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"TROUBLED PEOPLE ON THE JOB"

The title of this editorial is a pamphlet, prepared by the Committee on Occupational Psychiatry of the American Psychiatric Association under the chairmanship of Dr Ralph T Collins The Committee has sought to express psychiatric concepts in terms that would be understandable and recognizable to managers in industry who wish help in supervision of their employees, and for employees who "don t want help' or who refuse to recognize that they need help with emotional problems

Emotional disturbance is known to pose a serious threat to business in this country Emotional tensions among employees result in absenteeism and in accidents on the job A frequent complaint or justification for absenteeism is attributed to the common cold, headache, migraine, and gastrointestinal disturbance These excuses, although generally accepted, are probably more often direct effects of managerial mismanagement or misconception of supervision Troubled People on the Job" states that a boss who is troubled with anxiety, hopelessness, irresponsibility, hostility, or anger may communicate these feelings to his subordinates who in turn pass these reactions along, frequently with an increase in intensity The hope is expressed that some emotional tensions may be relieved by thoughtful and understanding supervisors

It is believed that there is need for indoctrination of industrial supervisors with the concept that sometimes an understanding of emotional problems may be a jobsaving or even a lifesaving measure Management will benefit by the appreciation of the fact that the employees are not necessarily cogs or wheels, but persons One deeply disturbed person can often 'infect" a whole department

Wide application of such concepts in handling employees not only benefits the employee but can also result in saving to business

MEDICAL NEWS

CALIFORNIA

Personal —Dr Edward Kupka, Berkeley, chief, Bureau of Tuberculosis Control, California State Department of Public Health, has taken a two-year leave of absence to accept a tour of duty with the World Health Organization He will carry out epidemiological studies and participate in tuberculosis control projects in South and Central America Dr Kupka's previous foreign assignments have been to Italy, Samoa, and French Indochina —— Dr Myron Prinzmetal, professor of medicine, University of California Medical School, gave the annual duPont Lectures in Wilmington, Del , on May 17 Sponsored by the Delaware Heart Association, Dr Prinzmetal spoke to the public in the afternoon and to the medical profession the same evening His topic was "Coronary Disease and Angina Pectoris"——Dr L Henry Garland, San Francisco, was awarded the honorary degree of doctor of medicine by the University College, Dublin, Ireland, on June 23

DISTRICT OF COLUMBIA

High School Students Participate on Research Teams —Twenty District high school juniors, 15 boys and 5 girls, were assigned summer research duties at the Georgetown University Medical Center June 30 Winners of scholarships offered by the university, they will serve as members of research teams from July 5 to Sept 2 The program was praised by Dr Louis M Orr, Past-President of the American Medical Association, and Surgeon General Leroy Burney, of the U S Public Health Service, as being "in the interest of students and the medical and dental professions" Those chosen for the summer work were elected from over 300 applicants

FLORIDA

Dr Rose Wins Art Award —Dr Ben-Henry Rose, of Miami Beach, won the first prize for oil portraiture with his "Chinese Beggar in the Outer Territories of Hong Kong" at the annual show of the American Physicians Art Association, held in conjunction with the A M A convention The painting also won the prize as the most popular exhibit by vote of all those attending the show

GEORGIA

Dr O'Rear Named Medical College President — Dr Harry B O'Rear has been appointed president of the Medical College of Georgia, Augusta The appointment was announced by the board of regents of the University System of Georgia Dr O'Rear served as acting president since July, 1958, when he was given an interim appointment following the retirement of Dr Edgar R Pund Dr O'Rear has been associated with the Medical College of Georgia since 1950, when he joined the faculty as professor of pediatrics Subsequently, he was made departmental chairman of pediatrics, and later was named dean of the school Dr O'Rear received his M D degree from the University of Pennsylvania School of Medicine, Philadelphia, in 1943 The new Medical College of Georgia president is a member of the board of directors of the Augusta Red Cross chapter and is serving as board chairman of the Augusta Episcopal Day School

Personal —Dr Rolla Eugene Dyer, Emory University, received an honorary doctor of science degree at the 99th annual Washington University commencement June 6 Dr Dyer was director of the National Institutes of Health and assistant surgeon general of the Public Health Service from 1942 to 1950, when he retired from active duty He organized and developed the research grants and fellowships division of the National Institutes of Health, which administers the research programs of the Public Health Service ——Dr Jack C Norris, Atlanta, president, Georgia Social Hygiene Council, and clinical associate professor of pathology Emory University, was selected to receive the AVEN Citizenship Award of the Fulton County Medical Society "for his continued leadership in civic as well as medical affairs"

ILLINOIS

Chicago

Swedish Researchers Receive Cancer Award —Drs Georg and Eva Klein have been named the recipients of the third annual award "for meritorious investigation by a scientist under the age of 45 in the field of cancer," given by the Ann Langer Cancer Research Foundation of Chicago Over $150,000 has been contributed by the foundation to the University of Chicago, Michael Reese Hospital, Mount Sinai Hospital, and the Hebrew University in Israel for cancer research work The

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health Programs should be received at least three weeks before the date of meeting award is being supported by the family of the late Bertha Goldblatt Teplitz, who resided on the South Side of Chicago Dr Georg Klein, head, Institute for Tumor Biology, Karolinska Institutet Medical School, Stockholm, and his wife, Dr Eva Klein, associate professor of medical cell research, Karolinska Institutet, received the award for their "classic studies in the genetic aspects of tumor growth" They will receive a $500 honorarium

Society News—At the annual meeting of the Chicago Society of Industrial Medicine and Surgery May 11, the following members were elected as officers for 1960-1961 president, Dr Richard E Heller, vice-president, Dr Richard A Perritt, secretary, Dr Bille B Hennan, and treasurer, Dr Charles M Drueck —The Chicago Surgical Society at its annual business meeting elected the following officers for the 1960-1961 season Dr Walter G Maddock, president, Dr Paul W Greeley, vice-president, Dr Paul V Harper Jr, treasurer, and Dr Stanley E Lawton, recorder

LOUISIANA

Pediatrics Seminar—The Louisiana chapter of the American Academy of Pediatrics and the American Academy of General Practice are sponsoring a seminar, "Advances in Pediatric Therapy," to be held Sept 23 in New Orleans "Immunization Procedures in Children,' "Aerosol Therapy in Chronic Pulmonary Disease of Children," "Treatment in Viral Disorders," 'Hypnosis in Medicine,' 'Cryptorchidism A Logical and Embryological Approach to Management," and 'Practical Use of Steroids in Childhood" are among the topics to be considered

MICHIGAN

Hospital Addition Planned—Mr Walter P Reuther, president, United Auto Workers, was guest speaker at the ground-breaking ceremonies for a $2,350,000 addition to Metropolitan Hospital June 19 Metropolitan Hospital, at 1800 Tuxedo, Detroit, is constructing a two-story building to be opened in the summer of 1961 The new building is to be featured in an architectural display at the American Hospital Association convention in San Francisco in August Features of the air-conditioned wing include a surgical suite with peripheral corridors and centralized operating room facilities, a new x-ray department, and 'a complete laboratory with the latest in electronic equipment' The addition will also contain a pharmacy, kitchen and dining facilities, and an emergency room The new clinic, along with proposed branch clinics, will provide offices for 75 full-time physicians Out-patient care will be provided, including psychiatry, physical medicine, allergy, and surgery Alterations on the present building will provide more office and administrative space, plus an additional 75 beds

Surgical Resident Competition Held—The ninth annual competition for the Frederick A Coller Award, sponsored by the Regional Committees on Trauma and Nutrition and the Michigan State Chapter of the American College of Surgeons, was held in Ann Arbor May 26 Twenty 10-minute papers were given by surgical residents from hospitals in Michigan and northern Ohio, topics included clinical and experimental studies on problems related to the surgical management of trauma and attendant nutritional problems First prize was awarded to Dr John Mitchell, of Wayne County General Hospital, Eloise, for his paper, 'A Clinical and Experimental Study of Pulmonary Contusion" Second and third prizes were given to Dr Robert Shanahan, of St Joseph Mercy Hospital, Ann Arbor, and Dr Charles Friend, of the Wayne County General Hospital, Eloise The program also included an address by the president of the American College of Surgeons, Dr Owen H Wangensteen, titled 'The Education of a Surgeon"

MINNESOTA

Air Pollution Study—The degree to which air pollution is an actual or potential problem in Minnesota will be studied in a state-wide survey being conducted by the Minnesota Department of Health with the cooperation of the U S Public Health Service The three-part survey includes questionnaires, community field visits, and air sampling at five stations Results of the survey should be available next October, according to Mr F L Woodward, director of the division of environmental sanitation Of the communities queried in the survey, more than half of those with a population of 1,000 or more stated that they had some air pollution problem The statewide survey will evaluate the problem on the basis of anticipated growth, climate, topography, and fuel use, and will provide information on the needs for state and local control and enforcement measures

MISSISSIPPI

Bat Bites Reported—The Morbidity Report of the Mississippi State Board of Health, for the week ended June 17, states that five persons living in one small area in a town in the north central part of the state were attacked by bats Physical examinations showed small, closely spaced, superficial punctures of the scalp at the point of contact Preliminary investigation indicated that the victims were struck by the mouse-eared, little brown bat Reports were received of four bats that had fallen to the ground in the week preceding the attacks Rabies in bats has not yet been identified in Mississippi

NEW YORK

Dr Brown Named Dean.—Dr Robert L Brown, assistant dean of the University of Buffalo School of Medicine, was appointed dean of the medical school The appointment is effective this month, and he will succeed Dr Ernest Witebsky Dr Brown, who will hold the rank of assistant professor, joined the UB medical staff in May, 1959 Prior to that time he was medical and technical director of the Arner Company, Inc He earned the MD degree at the University of Buffalo in 1944 and served as intern and assistant resident at Buffalo General Hospital 1944-1946

Annual Lecture Scheduled—The 11th Augustus B Wadsworth Lecture will be given at the Division of Laboratories and Research, New York State Department of Health, Albany, Oct 20 Dr Harry M Rose, chairman, department of microbiology, Columbia University College of Physicians and Surgeons, New York City, will present "A Prospect of Viral Infections of the Respiratory Tract" The lectureship was established in 1950 by the staff of the laboratories and the council of the New York State Association of Public Health Laboratories

Basic Science Research Building Dedicated—A new seven-story Basic Science Research Building, the first of two sections at Roswell Park Memorial Institute, Albany, the State Health Department's cancer research facility, was dedicated June 17 Principal speaker at the ceremonies was New York Governor Nelson A Rockefeller Among the participants were Dr Herman E Hilleboe, state health commissioner, and Dr George E Moore, Buffalo, director of Roswell Park Memorial Institute The $2,623,000 structure has more than 50 laboratories and a library with a capacity of more than 30,000 volumes The 120 members of the institute staff will carry on studies in physics, neurophysiology, steroid chemistry, radiobiology, biochemistry, experimental biology, and experimental pathology in the new structure

New York City

Dr. McIntosh Retires—Dr Rustin McIntosh, Carpentier Professor of Pediatrics, Columbia University College of Physicians and Surgeons, retired from the faculty on June 30, after more than 30 years of teaching In recognition of his career, he was appointed Carpentier Professor Emeritus of Pediatrics by the Columbia trustees He also retired from his position as attending pediatrician and director of the pediatric service at Babies (Presbyterian) Hospital at the Columbia-Presbyterian Medical Center, he now serves as consultant to Presbyterian Hospital Dr McIntosh graduated from Harvard Medical School, Boston, in 1918 He has been president of the Society for Pediatric Research (1934), American Pediatric Society (1953-1954), medical board of Presbyterian Hospital (1949-1952), and is the co-editor of "Holt's Diseases of Infancy and Childhood"

University News—A special lecture was delivered at the State University of New York Downstate Medical Center on June 1 by Dr Peter Bischoff, chief of urology, St Elizabeth's Hospital, Hamburg, Germany Dr Bischoff spoke on "Surgical Repair of Hydronephrosis and Megaloureter"——Dr Sylvester J Carter was promoted to director of the newly established Hand Surgery Service of New York Medical College The service is located at Metropolitan Hospital and became effective July 1 A member of the faculty of New York Medical College since 1959, Dr Carter received his MD degree from Boston University School of Medicine in 1939

Personal—Dr Edward H Ahrens Jr and Dr James G Hirsch have been promoted to the rank of professor and member of the Rockefeller Institute Dr Ahrens has been at the Rockefeller Institute since 1946, except for the period 1951-1952 when he was associated with the Babies Hospital He is chairman of the Metabolism Study Section of the U S Public Health Service Dr Hirsch has been on the faculty of the Rockefeller Institute for 10 years ——Dr Stephen Nordlicht, assistant professor of psychiatry, New York Medical College, will spend July and August on an investigative project in geriatrics in Japan for the World Medical Association ——Dr Harry Most Herman M Biggs Professor of Preventive Medicine and chairman of the department, New York University Medical Center, was appointed director of the Commission on Parasitic Diseases of the Armed Forces Epidemiological Board The appointment, for a two-year term, was effective July 1

NORTH CAROLINA

Faculty Promotions—The Bowman Gray School of Medicine, Winston-Salem, announced the promotions to the rank of full professor of Dr William H Boyce Jr, professor of urology, Dr Richard L Burt, professor of obstetrics and gynecology, and Dr R Winston Roberts, professor of ophthalmology Dr Boyce on July 1 replaced Dr Fred K Garvey as director of the section on urology Dr Burt received his degree of doctor of medicine from Harvard Medical School, Boston, and joined the faculty of the Bowman Gray School of Medicine in 1949 Dr Roberts completed his medical education at Duke University School of Medicine and has served as director of the section in ophthalmology since 1947

OKLAHOMA

Dr Williams Named Mental Health Commissioner —Dr T Glyne Williams, assistant professor of psychiatry and public health at Yale University, New Haven, Conn , is the new Commissioner of Mental Health for Oklahoma, replacing Dr Hayden Donahue, who resigned last fall for additional training and private practice Dr Williams previously held posts as director, Yale Pilot study for Psychiatric Administration, and consultant, Connecticut Department of Mental Health He received his medical degree from Vanderbilt University School of Medicine, Nashville, Tenn , and is certified by the American Board of Psychiatry and Neurology and by the American Psychiatric Association as a mental health administrator

OHIO

Society News —The Ohio Psychiatric Association, at its annual meeting May 18, elected the following officers for the coming year president, Dr Roger M Gove, Columbus, president-elect, Dr Ewing H Crawfis, Cleveland, secretary-treasurer, Dr Irwin N Perr, Cleveland, councillors, Dr Arnold Allen, Dayton, and Dr J Robert Hawkins, Cincinnati —— At a recent meeting of the Central Ohio Radiological Society, the following officers were elected president, Dr William H Crays, Springfield, vice-president, Dr William B Schwartz, Columbus, secretary-treasurer, Dr Robert L Friedman, Columbus, councillor, Dr Paul A Jones, Zanesville, and alternate, Dr George F Jones, Lancaster The society meets on the second Thursday of October, November, January, March, and May in Columbus

WEST VIRGINIA

Dr Jones Named Anesthesiology Chairman —The appointment of Dr Richard E Jones of Swarthmore, Pa , as professor of anesthesiology and chairman of the division of anesthesiology at West Virginia University was announced June 28 Dr Jones, who is on the faculty of the University of Pennsylvania School of Medicine, will assume his duties in Morgantown before the opening of the Teaching Hospital in August He is a native of Cincinnati and holder of both bachelor's and M D degrees from Ohio State University In 1953, he was a resident in anesthesiology at the University of Pennsylvania, Philadelphia, and has been a member of that department since Dr Jones is a diplomate of the American Board of Anesthesiology

WISCONSIN

Conference on Cell Organization —The second Conference on the Chemical Organization of Cells, Normal and Abnormal, will be held at the University of Wisconsin, Madison, Aug 25-27 Among the topics to be discussed are protein structure, function, and synthesis, abnormal hemoglobins, inter- and intracellular membranes, antibody formation, and the lymphoid, macrophage, plasma, and R-E cell series Dr J F A McManus, University of Alabama Medical Center, Birmingham, is chairman of the conference

Personal —Dr David E Green, professor of enzyme chemistry at the Institute for Enzyme Research, University of Wisconsin, presented "Mitochondrion and Biochemical Machines" as the annual Christian A Herter Lecture of the New York University School of Medicine, New York City, April 20 —— Dr Arlan Rosenbloom, Ventura, Calif , 1958 graduate of the University of Wisconsin Medical School, will leave America soon for Cambodia to participate in MEDICO The Medical International Cooperation Organization is a nongovernmental, nonsectarian, voluntary organization supported by private contributions which patterns its work after that of Dr Albert Schweitzer It has set up 17 medical service programs in 12 countries Dr Rosenbloom is one of 20 American doctors, nurses, and medical aides who will leave soon for MEDICO posts

GENERAL

Increase Fees for Radiology Board Examination — The American Board of Radiology announced that effective Jan 1, 1961, applications for examination in radiology, diagnostic roentgenology, or therapeutic radiology must be accompanied by the fee of $150 Reexamination and other fees will be raised in about the same proportion Dr H Dabney Kerr, Kahler Hotel, Rochester, Minn , is the board secretary

Heart Films Listed —A Directory of Cardiovascular Films for use as a guide to clinicians, investigators, medical school personnel, and others has been compiled by the American Heart Association The 106 page booklet includes a list and evaluation of 273 films, a list of film sources, and subject and author indices It is available for $1 from local heart associations or the American Heart Association, 44 E 23rd St , New York 10

Clinical Hypnosis Meeting in Miami Beach —The third annual scientific meeting of the American Society of Clinical Hypnosis will be held at the Deauville Hotel, Miami Beach, Fla , Aug 7-10 Over 30 scientific presentations are scheduled Daily luncheon conferences will be held in the specialties of dentistry, psychology, general practice, pediatrics, psychiatry, obstetrics and gynecology, surgery, and anesthesia Social functions for those attending and for their wives are planned For information, write the American Society of Clinical Hypnosis, 6770 N Lincoln Ave, Chicago 46

Cardiac Conference in Denver —The ninth Western Cardiac Conference will be held Aug 15-20 at the Phipps Auditorium, Denver, under the auspices of the Colorado Heart Association Included in the program are the following topics intracardiac shunts, cardiac failure, radiology, cardiac surgery, vascular surgery, vascular disease, hypertension, electrocardiography, atherosclerosis, and space medicine Category I credit by the American Academy of General Practice is available for the sessions For information, write the Colorado Heart Association, 1636 Logan St, Denver 3

Surgeons Plan World Tour —The International College of Surgeons' annual round-the-world clinical tour will take off from New York City Sept 18 for 55 days of surgical sight-seeing and be back in the U S for Thanksgiving The itinerary includes Paris, Athens, Beirut, Jerusalem, Cairo, Bombay, New Delhi, Bangkok, Manila, Hong Kong, Nagoya, Tokyo, Honolulu, and San Francisco The travelers will observe and discuss surgery in these cities as well as hold joint meetings with foreign chapters of the college There were 35 surgeons on the 1959 tour This year's tour will be led by Dr Walter F James, executive director of the International College of Surgeons For information, write the International College of Surgeons, 1516 Lake Shore Dr, Chicago 10

Canadian and American Surgeons Convene —A joint meeting of the Canadian and United States Sections of the International College of Surgeons will be held Sept 28-29 in Winnipeg, Manitoba, Canada Sectional meetings on anesthesia, urology, obstetrics and gynecology, orthopedics, and eye, ear, nose, and throat are planned, as are exhibits, social events, films, and a banquet Included among the topics for discussion are common-duct strictures, diseases of the esophagus, vesicovaginal fistulas, diverticulitis, jaundice, plastic surgery, cancer of the larynx, tumors and cysts of the neck, postoperative complications following gastrectomy, blood volume, and nonunion in fractures Dr Samuel S Peikoff, Winnipeg, Manitoba, Canada, is general chairman Correspondence may be sent to the International College of Surgeons, 608 Power Building, Winnipeg, Manitoba, Canada

Rhinologic Society to Meet in Chicago —The American Rhinologic Society will hold its sixth annual meeting at the Belmont Hotel, Chicago, Oct 8 Physicians are invited, there is no registration fee The guest of honor and one of the afternoon speakers will be Dr Henry L Williams, Mayo Clinic, Rochester, Minn, whose subject will be "Thirty Years of Experience in Rhinology" The dinner speaker will be Dr Morris Fishbein, Chicago, who will present "Fifty Years of Medical Progress" Two symposiums will be held in the morning "Nasal Pressure Tests" and "Choanal Atresia" Other addresses include "Implant Materials—Compatibilities —Antigenicities," "Review of Reports on Lyophilized Bone and Cartilage," "The Comparative Anatomy of the Nose," "Hormones in Rhinology," and "Anti-Inflammatory Agents—Basic Concepts" For information, write Dr Robert M Hansen, Secretary, American Rhinologic Society, 1735 N Wheeler Ave, Portland 17, Ore

First Meeting of Colon Surgeons —The first annual meeting of the Association for Colon Surgery was held in Miami, Fla, on June 12 The main purposes of this new organization are to permit intestinal surgeons, physiologists, and pathologists "to pool their experience and knowledge, to stimulate interest and research in the function and diseases of the colon and rectum among general surgeons, and to encourage adequate teaching of anorectocolonic function and diseases to medical students and residents in surgery" The organization will work with the American College of Surgeons and the American Board of Surgery The program presented by the members included 19 papers and two panel discussions titled "Adenomas and Their Malignant Potential" and "Sphincter-Saving Operations for Cancer of the Rectosigmoid" The officers for 1960-1961 are Dr Warren H Cole, Chicago, president, Dr John M Waugh, Rochester, Minn, president-elect, and Dr Robert Turell, New York City, secretary-treasurer The 1961 meeting will be held in New York City

Seminar Cruise to Virgin Islands —A Duke University medical postgraduate seminar cruise to the Virgin Islands and Puerto Rico has been scheduled for November Plans for the cruise were announced by Dr William M Nicholson, assistant dean of the Duke Medical School, Durham, in charge of postgraduate education This cruise will replace one which had been scheduled for the Baltic area in June and which was cancelled Physicians participating in the Virgin Islands cruise will sail from New York aboard the Swedish American Motorlines *Kungsholm* Nov 9 Stops will be made at St John and St Thomas in the Virgin Islands and at San Juan, Puerto Rico The cruise will terminate at New York Nov 18 The lectures will deal with subjects that include thyroid abnormalities, chemical treatment of cancer, arthritis, diabetes, and blood disease The program will provide 30 hours of

Category I credit by the American Academy of General Practice Information concerning the cruise may be obtained by writing to the Director of Postgraduate Education, Duke University Medical Center, Durham, N C

Annual Conference on Anesthesiology—The New England Society of Anesthesiologists will present its third annual conference, "Anesthesia at Home and Abroad," at the Mount Washington Hotel, Bretton Woods, N H, Sept 16-18 Topics to be considered are 'Anesthesia at Home" and "Anesthesia Abroad," under the second of which the following will be presented

Anesthesia in Austria, Dr Otto Mayrhofer, Vienna, Austria
Anesthesia in Sweden, Dr Torsten Gordh, Stockholm, Sweden
Anesthesia in Belgium, Dr Alexandre Goldblat, Brussels Belgium
Anesthesia in Denmark, Dr Henning Ruben, Copenhagen, Denmark
Anesthesia Abroad, Dr John Gillies, Edinburgh, Scotland

Other speakers include Dr Henry K U Beecher Boston, Dr Curtiss B Hickcox, Hartford, Dr John R Lincoln, Portland, Maine, and Dr Meyer Saklad, Providence, R I A golf tournament is planned, and the annual banquet will be held the evening of Sept 18 For information, write the New England Society of Anesthesiology, Mount Washington Hotel, Bretton Woods, N H

Soviets Renew Contract with Science Publisher—A contract covering the translation into English of 23 major Soviet scientific journals was renewed for 1960 and 1961 on June 17 by representatives of Mezhdunarodnaya Kniga and Consultants Bureau Enterprises, Inc, a New York publishing house, at 227 W 17th St The president of Consultants Bureau reported that the agreement guarantees the company exclusive English-translation rights for journals in the fields of chemistry, physics, biology, and medicine The original arrangement was made between the two concerns in 1958 for one year only, and reportedly was the first such agreement ever reached between an American publisher and the Soviet Union The 1958 contract was renewed for one year in 1959 Under the terms of the new two year agreement, the Soviet agency "facilitates advance receipt of Russian journals by the publisher, and is pledged to use all means at its disposal to prevent infringement of the exclusive translation rights by any third party" In return, Consultants Bureau is making a reasonable royalty payment" The journals covered in the agreement include *Biochemistry, Bulletin of Experimental Biology and Medicine, Proceedings of the Academy of Sciences of the USSR (Doklady), Microbiology, Pharmacology and Toxicology,* and *Antibiotics*

International Congress on Physical Medicine—The third International Congress of Physical Medicine will be held in Washington, D C, Aug 21-26, Dr Frank H Krusen, congress president, announced Dr Krusen is senior consultant and former head of physical medicine and rehabilitation at the Mayo Clinic, Rochester, Minn Delegates from 27 countries are scheduled to attend the sessions at the Hotel Mayflower The program will be devoted to clinical, remedial, preventive, and educational aspects of physical medicine and current methods employed in physical medicine and rehabilitation Phases of physical medicine to be discussed include the diagnosis, evaluation, and treatment of diseases of the skeletal muscles, arthritis, neuromuscular diseases, physiatric care, prevention and treatment of back defects, congenital handicaps causing physical disability, rehabilitation following amputation, and geriatric care of the disabled person Vice-President Richard M Nixon is third congress patron, serving as patroness is Mrs Nixon Previous congresses were in England in 1952 and in Denmark in 1956 Congress headquarters are in Chicago

Joint Health Conference in Minneapolis—The Schools of Public Health of the University of Michigan and the University of Minnesota will hold their third annual institute on Nov 28-Dec 2 in Minneapolis The institute, "Newer Concepts of Growth and Development Implications in Child Health," will consist of a series of seminars and discussions on such topics as the 1960 White House Conference, newer knowledge in growth and development, program planning and evaluation, and enlisting community support Faculty for the program will be drawn from Michigan's and Minnesota's Schools of Public Health Staff members to be sent to the conference will be chosen by each state in the Midwest, and their expenses will be paid for as part of the institute from funds provided by the Children's Bureau At least two physicians will be among the four staff members selected from each state For information, write Dr Donald C Smith, Associate Professor of Maternal and Child Health, University of Michigan School of Public Health, Ann Arbor, Mich, or Dr Gaylord W Anderson, Director, University of Minnesota School of Public Health, Minneapolis

Society News—**The Association of State and Territorial Public Health Laboratory Directors** elected the following officers to serve during 1960-1962 president, Elmer L Shaffer, Ph D, Trenton, N J, vice-president, Howard L Bodily, Ph D, Berkeley, Calif, secretary-treasurer, Melvin E Koons, M Sc, Grand Forks, N D, executive committee, Dr

Rochester, N Y, executive secretary-treasurer, Ray G Daggs, Ph D, Washington, D C, and administrative advisor, Milton O Lee, Ph D, 9650 Wisconsin Ave, Washington 14, D C——Dr Herbert Conway, of New York City, was elected president of the **American Association of Plastic Surgeons** at the association's annual business meeting May 19 He succeeds Dr Lyndon A Peer, of East Orange, N J Other officers elected by the group are Drs William H Frackelton, Milwaukee, vice-president, and Thomas D Cronin, Houston, Texas, reelected secretary-treasurer Dr William L White, Pittsburgh, was elected to a three-year term on the board of trustees

Students Win Foreign Fellowships—Twenty-eight American medical students, winners of Smith Kline & French Foreign Fellowships totaling some $50,000, will study diseases not commonly seen in America, when they go to three continents this summer and winter Guided by physicians already practicing in remote areas, the fellows will help to organize and maintain public health programs They also will represent American medical school education in areas where medicine often is practiced in primitive surroundings The fellowships were announced June 1 by the Association of American Medical Colleges, administrators of SK&F fellowships, in Evanston, Ill Chosen by a committee of medical educators selected by A A M C, the 28 fellows will receive individual grants ranging from $900 to $3,000 Two of the fellows received awards large enough to permit their wives, registered nurses, to participate in the work-study programs The fellowship program is made possible by a $180,000 grant from Smith Kline & French Laboratories, Philadelphia pharmaceutical firm During the three years of the planned program (through 1962) about 90 selected students who will have completed at least three years of medical school will receive financial grants to permit them to spend vacation periods studying in underdeveloped areas of their choice The locations in which students will work include Bolivia, Liberia, the Congo, Afghanistan, Nigeria, the Philippines, Southern Rhodesia, Thailand, Iran, India, Nepal, Libya, Peru, Uganda, Ethiopia, Union of South Africa, Java, and Ghana The students' stay at the overseas locations will be a combination of clinical work and observation

Report on United Nations Children's Fund—American boys and girls are getting ready to follow the example set 10 years ago by a few Sunday school pupils who donated their Halloween "treats" of coins to the United Nations Children's Fund Last fall, Trick or Treat for UNICEF, pennies, nickels, and dimes, totaled $1,500,000 There are 55,000,000 children and mothers who are receiving UNICEF aid in 107 countries this year UNICEF, the United Nations Children's Fund, established by the UN General Assembly as an agency concerned with children, works in four major ways to help meet their needs (The words "Emergency" and "International" were dropped from the fund's original title in 1953, but the name of UNICEF and its symbol, a child drinking a cup of milk, remain unchanged) UNICEF helps to alleviate problems of malnutrition by shipping powdered milk for distribution through schools and health centers, and by providing equipment for milk conservation plants UNICEF also helps to develop other foodstuffs rich in protein, locally available and suitable for children, including fish flour and flours from vegetable sources Assistance is given for the local training of nutrition workers who will help educate rural families in wise food practices, and tools and equipment are provided to encourage families to raise their own vegetables, poultry, small animals, or fish A second form of activity, aid to basic maternal and child health and welfare services, includes equipping some 23,000 health centers all over the world UNICEF helps governments to control and eradicate diseases that affect large numbers of children, including tuberculosis, malaria, yaws, trachoma, and leprosy In all these fields, UNICEF works closely with other UN agencies, especially with the World Health Organization and the Food and Agriculture Organization

Society News—The following officers were elected at the June meeting of the **Eastern Psychiatric Research Association, Inc**, to take office during the annual meeting to be held at the Waldorf-Astoria Hotel, Nov 4-5 president, Dr Charles Buckman, Kings Pk, N Y, president-elect, Dr William Malamud, Boston, first vice-president, Dr Emerick Friedman, Albany, N Y, second vice-president, Dr William Furst, East Orange, N J, secretary-treasurer, Dr David J Impastato, New York City, assistant secretary-treasurer, Dr Albert N Mayers, New York City, councilors, Drs William B Terhune, New Canaan, Conn, Wilfred Dorfman, Brooklyn, and Robert E Arnot, Boston——Dr William B Tucker, Washington, D C, succeeded to the presidency of the **American Thoracic Society**, medical section of the National Tuberculosis Association and formerly known as the American Trudeau Society Dr Robert H Ebert, Cleveland, was chosen president-elect, to take office next spring For the first time in the history of the 55-year-old society, a woman was named vice-president She is Dr Katharine R G Boucot, of Woman's Medical College, Philadelphia Elected also were secretary-treasurer, Dr Frederick C Waring Jr, Shelton, Conn (reelected), councelor-at-large, Drs William R Barclay, Chicago, Albert I C DeFriez, Boston, John C Ham, Providence, R I, John H McClement, New York City, and Randolph B Turnbull, Memphis, Tenn —On April 26, the American Proctologic Society elected the following officers for 1960-1961 president, Dr Walter A Fansler, Minneapolis, president-elect, Dr Merrell O Hines, New Orleans, vice-president Dr Robert T McCarty, Milwaukee, secretary, Dr Norman D Nigro, Detroit, and treasurer, Dr Robert J Rowe, Dallas, Texas The next annual meeting will be held June 21-24, 1961, at the Pittsburgh Hilton Hotel, Pittsburgh, and will be open to members and guests

FOREIGN

World Medical Association Meeting in West Berlin —The 14th general assembly of the World Medical Association will be held at the Berlin Congress Hall, West Berlin, Germany, Sept 15-22, in conjunction with the 63rd Deutche Arztetag The opening ceremonies will include addresses by Dr Renaud Lemieux, president of the association, Dr Ernst Fromm, president, Deutche Arztetag and treasurer of the W M A, Dr h c Heinrich Lubke, President of the Federal Republic of Western Germany, Dr Gerhard Schroder, home secretary of the Federal Republic, and Mr Willy Brandt, mayor of Berlin Prior to the keynote address by Dr Fromm and the opening of the technical exhibition, the president for 1960-1961 will be elected and installed

CORRECTION

Dosage of Methohexital Sodium —In the Council on Drugs monograph on methohexital sodium in The Journal, June 11, page 676, the last sentence under the section on Dosage" should read as follows 'When given by continuous intravenous drip to supplement other forms of anesthesia, a 0 2% solution is used"

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC

Educational Council for Foreign Medical Graduates Stations around the world Sept 21, 1960 Exec Director, Dr Dean F Smiley, 1710 Orrington Ave, Evanston, Ill

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners Part I, Various Cities, Sept 7-8 Part II Applications must be received at least six weeks before the date of the examination Exec Sec, Dr John P Hubbard, 133 South 36th St, Philadelphia

BOARDS OF MEDICAL EXAMINERS

Alaska * On application in Anchorage or Fairbanks Sec, Dr W M Whitehead, 172 South Franklin St, Juneau

California *Written* Los Angeles, Aug 22-25 and Sacramento, Oct 17-20 *Oral and Clinical* Los Angeles, Aug 21, and Los Angeles, Nov 29 *Oral for Reciprocity Applicants* San Francisco, June 18, Los Angeles, Aug 20 and Nov 19 Sec, Dr Louis E Jones, Room 536, 1020 N Street, Sacramento

Canal Zone On Application Acting Sec, Dr B K Levin, Health Bureau, Balboa Heights

Colorado * *Examination* Denver, Dec 13-14 Exec Sec, Miss Mary M McConnell, 715 Republic Bldg, Denver 2

Guam *Subject to Call* Sec, Dr F L Conklin, Agana

Montana *Examination and Reciprocity* Helena, Oct 4 Sec, Dr Thomas L Hawkins, 555 Fuller Ave, Helena

Nebraska * *Examination* Omaha, June Director, Bureau of Examining Boards, Mr R K Kirkman, Room 1009, State Capitol Bldg, Lincoln 9

Nevada *Examination and Reciprocity* Reno, Sept 7 and Dec 7 Sec, Dr G H Ross, 112 North Curry St, Carson City

New Hampshire *Examination and Reciprocity* Concord Sept 14-17 Sec, Dr Edward W Colby, 61 South Spring St, Concord

Ohio *Examination* Columbus, Dec 12-14 *Endorsement* Columbus, Aug 12 and Oct 4 Sec, Dr H M Platter, 21 W Broad St, Columbus 15

Puerto Rico *Examination* San Juan, Sept 6-10 Sec, Dr Herminio Mendez Herrera, Box 9156, Santurce

South Dakota * *Reciprocity* Continuously Exec Sec, Mr John C Foster, 300 First National Bank Bldg, Sioux Falls

Texas * *Examination and Reciprocity* Fort Worth, Dec 1-3 Sec, Dr M H Crabb, 1714 Medical Arts Bldg, Fort Worth 2

Washington * *Reciprocity* Continuously Administration, Mr Thomas A Carter, Capitol Bldg, Olympia

Wyoming *Written* Cheyenne, Oct 3 *Oral for Reciprocity Applicants* Cheyenne, Oct 3 Sec, Dr James W Sampson, State Office Bldg, Cheyenne

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Colorado *Examination and Reciprocity* Denver, Sept 7-8 and Dec 7-8 Sec, Dr Esther B Starks, 1459 Ogden St, Denver 18

Michigan *Examination* Ann Arbor and Detroit, Oct 14-15 Sec, Mrs Anne Baker, 116 Stevens T Mason Bldg, Lansing

Minnesota *Examination* Minneapolis, Oct 4-5 Sec, Dr Raymond N Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14

Nebraska *Examination* Omaha, June Director, Bureau of Examining Boards, Mr R K Kirkman, Room 1009, State Capitol Bldg, Lincoln 9

Oklahoma *Examination* Oklahoma City Sept 23-24 Exec Sec, Mrs L Haidek, Braniff Bldg, Oklahoma City

Wisconsin *Examination* Madison, Sept 9 Milwaukee Dec 10 Sec, Dr W H Barber, 621 Ransom St, Ripon

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*Basic Science Certificate required

GOVERNMENT SERVICES

AIR FORCE

Medical Aspects of Space Operations.—A group of medical officers from the Army, Navy, and Air Force were given an intensive two-week course in space medicine at the Air Force Missile Test Center Col George M Knauf was responsible for setting up the course The new course will be offered on a continuing basis at the AFMTC Its purpose is to make available a pool of qualified medical officers from the three services who will be able to function as space surgeons to support future requirements of Project Mercury and other man-in-space programs Thirty-eight key medical instructors from the three services, other governmental agencies, and private industry will teach subjects ranging from a history of astronautics to acceptable metabolic aberrations in space operations About 50 medical officers will take this space surgeon training each year

ARMY

General Shambora Honored.—Major Gen William E Shambora, Commanding General of Brooke Army Medical Center, was one of three prominent Americans awarded an honorary degree of Doctor of Laws at the 1960 commencement of St Mary's University in San Antonio, Texas

Retirement.—Col Joseph M Cameron, who for almost eight years has been the senior medical officer at the U S Army at Chemical Corps School at Fort McClellan, Ala , was retired on June 30 He was awarded the Bronze Star medal and the Purple Heart in World War II

VETERANS ADMINISTRATION

Body Radiation Counter.—An instrument known as a human-body radiation counting system was installed at the Veterans Administration center in Los Angeles The 25-ton steel room, with instrumentation, makes possible measurement of the amount of radiation present in the body from fallout, medical dosage, handling radioactive materials, or other sources It will be used in diagnosis and medical research and will be an important resource for civil defense It is the second such installation in the VA and brings to about six the number of such radiation counting systems in the United States Each of these was individually designed and constructed The counter at the Los Angeles center was designed by Drs William H Blahd, Benedict Cassen, and Norman MacDonald

The VA's other total-body radiation counter is at the agency's hospital in Boston The Boston hospital is now in the process of installing around its counter 175 tons of surplus steel armor plate, obtained from the Navy The shielding is necessary to screen out radiation from outside sources, so that so far as possible only the radiation from the body of the person undergoing testing is counted

The steel chamber for the Los Angeles counter is 6 by 6 by 4 feet in size and is made of five laminated 1-in sheets of steel, plus a 1/16-in lead lining It is housed in a steel building, which is insulated and air conditioned In testing, the patient sits in the chamber Mounted over him is an extremely sensitive detector which transmits the radiation measurement to an analyzer mounted outside the steel chamber It is possible with this counter to measure the natural human radioactivity emanating from body potassium Knowledge of body potassium content is of importance in diagnosis of diseases involving the nerves, muscles, and kidneys

PUBLIC HEALTH SERVICE

Personal.—Dr Kenneth R Nelson, formerly chief of the division of hospitals, became chief medical officer of the U S Coast Guard, effective July 1 He succeeded Dr Richard B Holt, who retired because of physical disability Dr Myron D Miller, formerly deputy chief of the division of hospitals, became the new chief of that division

Dietary Aspects of Cardiovascular Diseases.—A new pamphlet, "Dietary Aspects of Cardiovascular Diseases—Selected References," has been published The references were compiled for professional health personnel who need current information and teaching materials on the dietary aspects of cardiovascular diseases It should also be useful to many private physicians, voluntary health workers, and others Copies of this reference list may be obtained by professional workers at no cost from the Heart Disease Control Program, U S Public Health Service, Washington 25, D C

Biologics Standards Building.—The Division of Biologics Standards building of the National Institutes of Health in Bethesda, Md , was dedicated on June 30, in ceremonies at which Surgeon General Leroy E Burney presided King Bhumibol Adulyadj of Thailand, Secretary of Health, Education, and Welfare Arthur S Flemming, and Dr James A Shannon, director of NIH, took part in the program The building was specially designed to house the scientific and administrative operations of the division, which is responsible for the safety, purity, and potency of all biological products within the jurisdiction of the Public Health Service

DEATHS

Greenberg, Morris Ⓜ New York City, born in Rumania in 1890, Columbia University College of Physicians and Surgeons, New York City, 1917, director of the Bureau of Preventable Diseases of the New York City Health Department, specialist certified by the American Board of Pediatrics and the American Board of Preventive Medicine, member of the American Academy of Pediatrics, past-president of the New York Pediatric Society, served as associate professor of epidemiology at the Columbia School of Public Health and Administrative Medicine, recipient of many honors, among which was the 1955 medical citation of the Citizens Budget Commission, consulting physician at the Knickerbocker Hospital, from 1926 to 1943 attending pediatrician at the New York Nursery and Children's Hospital, and from 1936 to 1942 was with Gouverneur and Sydenham hospitals in similar capacities, from 1938 to 1955 was with Beth David Hospital, author of several books, died in the New York Hospital May 25, aged 69, of acute myocardial infarction

Groom, Corwin Peter, Pocatello, Idaho, Northwestern University Medical School, Chicago, 1909, associated with the Bannock Memorial and St Anthony Mercy hospitals, died May 10, aged 77, of diabetes

Hagler, Frederic, Springfield, Mass , Washington University School of Medicine, St Louis, 1910, fellow of the American College of Surgeons, president of the Massachusetts Medical Society, 1953-1954, past-president of the Hampden District Medical Society and the Springfield Academy of Medicine, a Red Cross surgeon with the American Red Cross in Belgrade, Serbia, in 1915, for which he was decorated, and with the Red Cross unit in Graudenz, Germany, in 1916, veteran of World War I, served as trustee of the Springfield Municipal Hospital and past-president of the medical staff of the Wesson Memorial Hospital, where he died May 13, aged 72, of coronary thrombosis

Herrick, Jessie Louise, Denton, Texas, Woman's Medical College of Pennsylvania, Philadelphia, 1895, for many years physician at the Texas State College for Women, where she organized the health service, past-president of the American Student Health Association, died in the Flow Memorial Hospital May 15, aged 96, of bronchopneumonia with associated cardiovascular renal failure

Hinden, Jacob, Strong City, Kan , Kansas Medical College, Topeka, 1902, served as mayor, member of the school board, and county coroner, died in the Newman Memorial County Hospital, Emporia, May 21, aged 86, of generalized arteriosclerosis

Hirwas, Charles Leonard Ⓜ Marquette, Mich , University of Michigan Medical School, Ann Arbor, 1926, fellow of the American College of Surgeons, on the staff of St Luke's Hospital, died in St Mary's Hospital May 16, aged 61, of carcinoma of the colon with metastasis to liver and lungs

Howard, Hector Holdbrook, Jackson, Miss , Memphis (Tenn) Hospital Medical College, 1910, appointed director for the West Indies of the International Health Board of Rockefeller Foundation in 1914 and in 1927 was named associate director, serving until 1934, when he retired, author of many publications on disease control, died May 10, aged 86, of nephrosclerosis

Huffman, Charles S Ⓜ Columbus, Kan , born in Vincennes, Ind , Oct 8, 1865, Missouri Medical College, St Louis, 1890, for many years secretary of the Kansas Medical Society, of which he was past-president, named "Kansas Doctor of the Year", veteran of the Spanish-American War, served as a brigadier general in the Kansas National Guard, formerly lieutenant governor and state senator, for four years member of the state board of health, at one time editor and associate editor of the *Journal of the Kansas Medical Society,* president and director of the Columbus State Bank, a director of the Preferred Fire Insurance Company of Topeka, died in the Maude Norton Memorial City Hospital May 6, aged 94, of hypostatic pneumonia

Hughes, E Charles Ⓜ Bay City, Mich , University of Louisville (Ky) Medical Department, 1894, served on the staffs of the Mercy and General hospitals, died in the Bay City Samaritan Hospital May 14, aged 87, of paralysis agitans

Hyde, Burton Edward Long Ⓜ Troy, Ohio, University of Michigan Medical School, Ann Arbor, 1925, served on the faculty of his alma mater, veteran of World War II, associated with the Dettmer Hospital and the Stouder Memorial Hospital, died May 18, aged 60, of injuries received in an automobile accident

Jurek, Ladislaus Joseph Ⓜ Antioch, Ill , Chicago Medical School, 1935, veteran of World War II, member of the American Academy of General Practice, associated with the Mercy Hospital in Chicago, died May 31, aged 59, of acute coronary occlusion

Kalisz, Walter Frederick, Chicago, Loyola University School of Medicine, Chicago, 1916, member of the American Academy of General Practice, vet-

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Ⓜ Indicates Member of the American Medical Association

eran of World War II, senior staff member of St Elizabeth Hospital, died in Elgin, Ill, May 28, aged 69, of coronary occlusion

Kelley, Edward Theron, Georgetown, S C, Medical College of the State of South Carolina, Charleston, 1908, fellow of the American College of Surgeons, died May 16, aged 73, of acute coronary occlusion

Kinkead, Kyle Johnston Ⓜ Birmingham, Ala, Tulane University of Louisiana School of Medicine, New Orleans, 1915, fellow of the American College of Physicians, past-president of the Jefferson County Medical Society, served on the faculty of the Medical College of Alabama, associated with St Vincent's Hospital and the University Hospital, where he died May 18, aged 72, of aortic aneurysm

Lane, Wilson Hewette Ⓜ Oklahoma City, Okla, Chicago College of Medicine and Surgery, 1913, member of the American Academy of General Practice, past-president of the Pontotoc County Medical Society, associated with Deaconess and Mercy hospitals and the Baptist Hospital, where he died May 16, aged 81, of carcinoma of the right kidney

Leary, Jeremiah Arthur, Cincinnati, University of Cincinnati College of Medicine, 1925, for many years on the staff of the Good Samaritan Hospital, a director of the First National Bank of Hyde Park, died May 24, aged 60, of pulmonary embolism

Lemire, Robert Wilfred Ⓜ Sedalia, Mo, St Louis University School of Medicine, 1950, interned at the Pima County General Hospital in Tucson, Ariz, served a residency at St Vincent Charity Hospital in Cleveland, Veterans Administration Hospital in Buffalo, and the Millard Fillmore Hospital in Buffalo, on the staff of the Bothwell Hospital, died in Chattanooga, Tenn, May 13, aged 41, of myocardial infarction

Leon, Harry George, Chicago, Loyola University School of Medicine, Chicago, 1919, formerly coroner's physician of Cook County, and was associated with the Illinois Masonic Hospital, died in Los Angeles May 26, aged 70, of arteriosclerotic heart disease

Levy, Louis Henry, New York City, Yale University School of Medicine, New Haven, Conn, 1911, served on the staff of the Mount Sinai Hospital, where he died May 26, aged 77, of coronary thrombosis

Lillehei, Elmer Julius Ⓜ Robbinsdale, Minn, University of Minnesota Medical School, Minneapolis, 1925, member of the American Academy of General Practice, on the staff of St Barnabas Hospital in Minneapolis, died in Minneapolis May 14, aged 65, of coronary thrombosis

Lockwood, Edward Kenton Ⓜ Springfield, Ill, Marion-Sims College of Medicine, St Louis, 1895, died in the Hollywood (Fla) Hospital May 13, aged 90, of fracture of the left femur, with pneumonia

Lynch, Leo Augustine Ⓜ Brooklyn, Johns Hopkins University School of Medicine, Baltimore, 1903, associated with the Swedish Hospital, died May 27, aged 81, of coronary occlusion

McKay, William Peter Ⓜ Fayetteville, N C, Tulane University School of Medicine, New Orleans, 1916, veteran of World War I, associated with Cape Fear Valley Hospital and the Highsmith Hospital, died May 21, aged 69, of coronary occlusion

Manis, Benedict Vincent, Coatesville, Pa, New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1934, interned at the Metropolitan Hospital, Welfare Island, New York City, where he served a residency, associated with the Coatesville Hospital, died in the Graduate Hospital of the University of Pennsylvania, Philadelphia, May 12, aged 50, of multiple peritoneal abscess following operation for duodenal ulcer

Maroney, Joseph Patrick, Boston, Tufts College Medical School, Boston, 1908, formerly associated with the New England Telephone & Telegraph Company, at one time chief of staff at Mercy Hospital in Springfield, died May 7, aged 81, of pneumonia

Mattes, Charles Louis, Webster Groves, Mo, St Louis University School of Medicine, 1914, medical director of the Reliable Life Insurance Company, of which he was co-founder and chairman of the board, died in St Joseph Hospital, Kirkwood, May 9, aged 77, of coronary atherosclerosis

Mayes, Dibrel Crowder, Church Road, Va, University College of Medicine, Richmond, 1905, died May 21, aged 79, of a heart attack

Menard, Marvin C, Cincinnati, University of Cincinnati College of Medicine, 1929, surgeon for the city police department, associated with the Cincinnati General Hospital and the Jewish Hospital, where he died May 27, aged 56, of subdural hematoma

Morris, Dowling C, Chattanooga, Tenn, University of the South Medical Department, Sewanee, 1905, died in the Newell Hospital May 15, aged 79, of a heart attack and diabetes

Morton, Dudley Joy, New York City, born in Baltimore March 27, 1884, Hahnemann Medical College and Hospital of Philadelphia, 1907, veteran of World War I, served on the faculty of his alma mater, instructor in surgery, orthopedic division, Yale University Medical School, New Haven, Conn, from 1924 to 1927 and assistant professor, 1927-

1928, from 1925 to 1928 on the staff of the New Haven Hospital, later associate professor of anatomy at Columbia University College of Physicians and Surgeons, research associate of the American Museum of Natural History, a charter member, secretary, and treasurer of the Association of Physical Anthropologists, author of several books, died in the Roosevelt Hospital May 22, aged 76, of cancer of the sigmoid with metatases to the liver

Mott, Joseph Ernest Ⓜ Paterson, N J , University and Bellevue Hospital Medical College, New York City, 1931, secretary of the Passaic County Medical Society, served as a member of the board of health of Paterson, associated with the Paterson General and St Joseph hospitals, veteran of World War II, held the American Theater and Asiatic Pacific ribbons with one star, the Philippines Liberation Ribbon, and the Victory Medal, editorial consultant of the *Bulletin of the Passaic County Medical Society,* died in Clifton May 24, aged 53, of arteriosclerotic heart disease

Muirhead, William Perry, Armonk, N Y , Queen's University Faculty of Medicine, Kingston, Ont , Canada, 1926, physician for the Consolidated Edison Company, member of the Industrial Medical Association, for many years practiced in Brooklyn, where he was on the staff of St John's Hospital, died May 27, aged 63, of cancer

Murray, Alfred Nicholas, Evanston, Ill , born in Bloomington, Jan 28, 1873, Rush Medical College, Chicago, 1901, past-president of the Chicago Ophthalmological Society, at one time on the faculty of his alma mater, served as page in the U S House of Representatives, 51st and 52nd congresses, on the medical advisory board, Selective Service, Chicago, during World War I, fellow of the American College of Surgeons, associated with the Ravenswood and Augustana hospitals in Chicago, eye, ear, nose and throat surgeon at the Children's Memorial Hospital and attending consultant in diseases of the eye, ear, nose and throat, U S Public Health Service Hospital in Chicago, author of "Minor Ophthalmic and Aural Technique and "A System of Ophthalmic Therapeutics", collaborator on anatomy in Woods American Encyclopedia of Ophthalmology, died in the Evanston Hospital May 26, aged 87, of carcinoma of the palate

Myers, Wade Cooper, Tampa, Fla , Atlanta School of Medicine, 1910, associated with the Tampa General, St Joseph's, and Centro Asturiano hospitals, died May 16, aged 72, of cerebral thrombosis

Owen, Joseph Allen Jr , Yountville, Calif , University of California School of Medicine, San Francisco, 1916, formerly served in the regular U S Navy, died May 2, aged 68, of nephrosclerosis with uremia

Polk, Florence Knouff, Drexel Hill, Pa , University of Pennsylvania School of Medicine, Philadelphia, 1924, served as director of the Hospital of the Woman's Medical College of Pennsylvania and of the laboratory at Abington (Pa) Memorial Hospital, associated with the health division of the Upper Darby school system, died May 25, aged 68, of coronary disease

Rayer, Kenneth Nichols Ⓜ New Orleans, Tulane University School of Medicine, New Orleans, 1927, veteran of World War II, served on the faculty of his alma mater and the Loyola University School of Dentistry, died May 20, aged 58

Robertson, J Churchill, Salem, Va , Medical College of Virginia, Richmond, 1923, member of the American Trudeau Society, affiliated with the Roanoke Memorial, Lewis Gale and Jefferson hospitals, and consultant in chest diseases at the Veterans Administration Hospital in Roanoke, Va , died in Roanoke May 4, aged 62, of a heart attack

Routley, Eric Francis, Long Beach, Calif , University of Toronto Faculty of Medicine, Toronto, Ont , Canada, 1943, interned at the Toronto General Hospital in Toronto, Ont , Canada, served a fellowship in surgery at the Mayo Foundation in Rochester, Minn , specialist certified by the American Board of Surgery, fellow of the American College of Surgeons, served with the Royal Canadian Army during World War II, associated with St Mary s Long Beach and Community hospitals, died May 25, aged 39, of acute cerebral infarction

Russell, John Thomas Ⓜ Annapolis, Md , University of Maryland School of Medicine, Baltimore, 1909, medical examiner for the county selective service board during World War II, for many years medical examiner for the Metropolitan Life Insurance Company, served on the staff of the Emergency Hospital, died May 22, aged 79, of cerebral hemorrhage

Rutz, Lawrence Magnus, Marcellus, Mich , University of Michigan Medical School, Ann Arbor, 1923, served as director of the Hospital of Southern Michigan Prison in Jackson, medical rating specialist for the Veterans Administration in Detroit, died in Detroit May 10, aged 61, of acute coronary occlusion

Sampson, David Moody, Pasadena, Calif , Columbia University College of Physicians and Surgeons, New York City, 1955, interned at the Bellevue Hospital Center in New York City, certified by the National Board of Medical Examiners, served in the regular U S Navy, died May 24, aged 28

Sampson, Frank Ernest Ⓜ Creston, Iowa, Rush Medical College, Chicago, 1891, honorary president and for many years president of the Union County Tuberculosis and Health Association, founder of

Greater Community Hospital, where he died April 21, aged 93, of bronchopneumonia

Schaffarzick, William Robert Ⓜ Baton Rouge, La.; born in Lake Mills, Wis., Aug. 25, 1918; Vanderbilt University School of Medicine, Nashville, Tenn., 1943; interned at the Vanderbilt University Hospital in Nashville, Tenn., where he served a residency at the Veterans Administration Hospital; veteran of World War II; formerly associated with the Veterans Administration Hospital and the Nashville General Hospital in Nashville, Tenn.; specialist certified by the American Board of Surgery; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; associated with Our Lady of the Lake Hospital and the Baton Rouge General Hospital, where he died May 21, aged 41, of coronary occlusion.

Schaller, Hans G. K. O., Poughkeepsie, N. Y.; Medizinische Akademie Dusseldorf, Dusseldorf, Germany, 1936; senior psychiatrist at the Hudson River State Hospital; died in St. Francis Hospital, Trenton, N. J., April 10, aged 48, of acute myocardial infarction.

Schmidt, Karl Henry, Minneapolis; Northwestern University Medical School, Chicago, 1903; veteran of World War I; died in the Veterans Administration Hospital Feb. 2, aged 79, of bilateral adrenal hemorrhage, bronchopneumonia and lung abscess.

Scott, Walter Roger Ⓜ Niagara Falls, N. Y.; Syracuse University College of Medicine, 1921; specialist certified by the American Board of Radiology, Inc.; fellow of the American College of Physicians; served on the staff of the Niagara Memorial Hospital; died May 21, aged 62, of hypertension.

Selman, Guy Stokely, Washington, Ga.; Atlanta School of Medicine, 1908; veteran of World War I; died May 6, aged 73, of coronary occlusion.

Shannon, Anne Lardner Moore Ⓜ Montclair, N. J.; Cornell University Medical College, New York City 1924; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served as vice-president of the Montclair Board of Education; formerly on the medical staff of the Metropolitan Life Insurance Company in New York City; on the staffs of the Montclair Community and Mountainside hospitals; died May 5, aged 61, of ovarian adenocarcinoma.

Shreehan, Hubert Francis, Newark, N. J.; George Washington University School of Medicine, Washington, D. C., 1934; veteran of World War II; associated with St. Michael's and St. James hospitals; died in St. Michael's Hospital May 7, aged 49, of cardiac failure.

Sights, Warren Preston, Paducah, Ky.; Rush Medical College, Chicago, 1915; member of the Industrial Medical Association; past-president of the McCracken County Medical Society; served on the faculty of his alma mater; veteran of World War I; on the staff of the Riverside Hospital; died May 17, aged 72, of carcinoma of the prostate and coronary heart disease.

Silvis, Richard Shippen Ⓜ Rear Admiral, U. S. Navy, retired, Castro Valley, Calif.; University of Nebraska College of Medicine, Omaha, 1931; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; entered the U. S. Navy in 1931 and retired Dec. 1, 1956; veteran of World War II and was awarded the Silver Star Medal for gallantry in action; from 1952 to 1956 chief of surgery at the U. S. Naval Hospital in Oakland; died May 5, aged 53, of acute hepatitis.

Skinner, Peter Searle, Bangor, Maine; McGill University Faculty of Medicine, Montreal, Que., Canada, 1926; associated with the Eastern Maine General Hospital and St. Joseph's Hospital; died May 5, aged 61, of acute coronary occlusion.

Smith, Paul Norton Ⓜ Oxnard, Calif.; born in Fargo, N. D., May 22, 1906; Rush Medical College, Chicago, 1936; interned at the Bellevue Hospital in New York City; served a residency at the Trudeau (N. Y.) Sanatorium, Olive View (Calif.) Sanatorium, and the Los Angeles County Hospital in Los Angeles; member of the American Academy of Dermatology and Syphilology, American College of Chest Physicians, and the American Trudeau Society; treasurer of the Ventura County Tuberculosis and Health Association; died May 7, aged 54, of acute myocardial infarction.

Soukup, Frank Kermit Ⓜ Captain, U. S. Navy, retired, Los Angeles; Western Reserve University School of Medicine, Cleveland, 1921; entered the U. S. Navy on Dec. 22, 1930, and retired Jan. 1, 1947; director of the Civil Service Department, Los Angeles City Health Department; died in the Crenshaw Hospital May 13, aged 64, of congestive heart failure.

Spencer, James Montrose, Roanoke, Va.; Medical College of Virginia, Richmond, 1916; died May 6, aged 69, of congestive heart failure.

Sprecher, Milford Harsh Ⓜ Elkton, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1931; on the staffs of the Memorial Hospital, Wilmington, Del., and Union Hospital; died May 18, aged 54, of coronary occlusion.

Stoliarsky, Raphael Grigonevich, New York City; Russian University of Warsaw Faculty of Medicine, 1920; formerly affiliated with Israel Zion Hospital in Brooklyn, died in the Grand Central Hospital May 29, aged 66, of acute coronary occlusion

Stoll, Edward Manning, Long Beach, Calif , University of Nebraska College of Medicine, Omaha, 1941, interned at the Eloise Hospital and Infirmary in Eloise, Mich , served a residency at the Henry Ford Hospital in Detroit, veteran of World War II, associated with the Seaside Memorial Hospital, Long Beach Community Hospital, and St Mary's Hospital, where he died May 9, aged 46, of bronchogenic carcinoma

Sullivan, Denis Timothy Joseph, Lansdowne, Pa , University of Pennsylvania School of Medicine, Philadelphia, 1921, member of the American Academy of General Practice, past-president of the Delaware County Medical Society, served as health officer of East Lansdowne, on the staff of the Delaware County Hospital in Drexel Hill and the Fitzgerald-Mercy Hospital in Darby, where he died May 18, aged 63, of pulmonary embolism

Swaney, Hugh Martin, Klamath Falls, Ore , St Louis University School of Medicine, 1938, on the staffs of the Klamath Valley and Hillside hospitals, accidentally drowned May 18, aged 49, while fishing in the Klamath River

Take, John Francis Ⓜ French Lick, Ind , Bennett Medical College, Chicago, 1889, member of the American Academy of General Practice, died in West Baden Springs May 12, aged 96, of cerebral hemorrhage

Tharp, Herbert Milton Ⓜ Monroe, Iowa, University of Illinois College of Medicine, Chicago, 1920, served as city health officer, affiliated with the Skiff Memorial Hospital in Newton, Iowa Methodist Hospital and the Iowa Lutheran Hospital in Des Moines, where he died May 6, aged 75, of malignancy

Timon, Alonzo N Ⓜ Los Angeles, Vanderbilt University School of Medicine, Nashville, Tenn , 1921, veteran of World War I, died May 13, aged 63, of coronary thrombosis

Titsworth, Sydney Ross, New York City, Columbia University College of Physicians and Surgeons, New York City, 1906, veteran of World War I, died in the Englewood (N J) Hospital April 19, aged 82, of cerebral hemorrhage

Toney, Lee Egbert, Piedmont, Mo , University of Louisville (Ky) Medical Department, 1907, veteran of World War I, served on the staff of the Veterans Administration Hospital in Little Rock, Ark , died May 16, aged 78, of cancer of the lung

Townsend, De Wayne, Brooten, Minn , Harvard Medical School, Boston, 1915, died in Macomb, Ill , May 5, aged 71, of coronary thrombosis

True, Augusta Isabella, Shawnee, Okla , University of Minnesota College of Medicine and Surgery, Minneapolis, 1894, died in the Anderson Carson and Hughes Hospital May 12, aged 96, of cerebral hemorrhage

Wallace, E Basse, Las Vegas, Nev , Ohio State University College of Medicine, Columbus, 1926, veteran of World War II, served on the staffs of the Boulder City (Nev) Hospital and the Southern Nevada Memorial Hospital, where he died April 28, aged 58, of myocardial infarction

Wallace, William Vincent, Port Arthur, Texas, University of Michigan Medical School, Ann Arbor, 1927, chief of the public health service, veteran of World Wars I and II, president of the Port Arthur Kiwanis Club, died May 12, aged 64, of subarachnoid hemorrhage

Walthall, Damon Orian, Kansas City, Mo , University of Michigan Medical School, Ann Arbor, 1916, specialist certified by the American Board of Pediatrics, member of the American Academy of Pediatrics, veteran of World War I, assistant clinical professor of pediatrics at the University of Kansas School of Medicine, associated with the St Luke's, Trinity Lutheran, St Mary's, and Kansas City General hospitals, died May 11, aged 70

Weiss, Morris Jacob Ⓜ Bayonne, N J , University and Bellevue Hospital Medical College, New York City, 1913, fellow of the International College of Surgeons, veteran of World War I, from 1915 to 1926 served first as a school physician and then as chief medical inspector of the board of education, associated with the Bayonne Hospital, died May 15, aged 70, of acute coronary thrombosis

Wenner, Richard Christian, Hamburg, Pa , University of Pennsylvania School of Medicine, Philadelphia, 1931, member of the American Trudeau Society, member of the medical staff at Hamburg State School and Hospital, where he died May 11, aged 55, of cerebral embolism

Wharton, Jesse Lawrence, Depew, Okla , Memphis (Tenn) Hospital Medical College, 1904, served on the staff of the Oklahoma State War Veterans Home Facilities in Sulphur, died in the Bristow (Okla) Memorial Hospital May 4, aged 86, of a fractured hip

Wilkinson, Levi Jennings Ⓜ Marshalltown, Iowa, State University of Iowa College of Medicine, Iowa City, 1907, past-president of the Marshall County Medical Society, on the staffs of the Evangelical and Mercy hospitals, died May 5, aged 82, of thromboangiitis obliterans

Wilson, Edgar Morris, Ashley, Ohio, Miami Medical College, Cincinnati, 1897, died in Mount Gilead May 15, aged 91, of uremia

FOREIGN LETTERS

BELGIUM

Contraindications to Drugs for Pilots and Drivers — Dr Evrard (*Bruxelles Médical*) listed the dangers of certain drugs which are administered to pilots of airplanes These dangers are of particular importance to fighter pilots, especially those who fly without co-pilots Even if a co-pilot is present, the pilot of a military or commercial plane is often responsible for the lives of many persons Dr Evrard's list included (1) antihistaminic drugs given to prevent motion sickness, (2) nasal mucosal vasoconstrictors, (3) antimalarial drugs, (4) drugs belonging to the atropine and scopolamine group, (5) antibiotics, because of their possible untoward effect on hearing and equilibrium, (6) sulfonamides, (7) stimulating drugs which affect the judgment, and, (8) relaxants or tranquilizers The author stressed the fact that, furthermore, these drugs should not be taken by persons who expect to drive an automobile Observance of these warnings should help to reduce traffic accidents

Two-stage Anesthesia Used in Cesarean Section — At the department of anesthesiology of the Belgian Society for Surgery, De Castro and Mundeleer reported a two-stage method of anesthesia used in a series of 18 cesarean sections All anesthetic agents enter the placental circulation Drugs with curare-like effect do not exert a special effect on the fetus The injection of neuroleptic drugs or of opiates, on the other hand, has a depressive effect on the neonate at birth

The first stage in the authors' method consisted of an injection of chlorethiazol followed by a perfusion with a solution of succinylcholine and the administration of nitrous oxide in 40% oxygen Tracheal intubation was performed, and when possible artificial respiration was applied with the aid of a mechanical device After delivery, a second solution consisting of procaine, Hydergine, and R 1406 as an analgesic, and haloperidol as a neuroleptic and antiemetic, was injected The results were excellent in the mother as well as in the newborn infant

BRAZIL

Lobectomy for Bronchial Cancer —Lobectomy for the treatment of bronchial cancer is preferred to pneumectomy as it is less radical Jatene and Zerbini (*Rev méd brasil* 5 434, 1959) studied a series of 262 patients with bronchial carcinoma In this series, 78 patients (29 8%) were considered inoperable, 87 (33 2%) were subjected to thoracotomy, during the performance of which contraindication of resection was verified, and 97 (37%) had pulmonary resections (74 pneumectomies and 20 lobectomies) The percentage of patients in whom resection was possible increased from 25% in 1949 to 33% in 1954 as a result of the improvement in diagnostic and surgical techniques Of the 74 patients who had pneumectomies, 16 died, but among the 20 patients who had lobectomies, there were no deaths Survival for five years occurred in 2 (2 7%) of those who had pneumectomies and in 5 (25%) of those who had lobectomies The authors urged that, if there is a shadow in the x-ray picture and cancer cannot be ruled out, thoracotomy should always be performed

CANADA

Bretylium Tosylate —Bretylium tosylate, a new antihypertensive agent, has a selective blocking action on the peripheral orthosympathetic nerves, resembling that which occurs after section of adrenergic nerves It has little or no significant effect on parasympathetic function Genest and co-workers (*Canad M A J* 82 872, 1960) gave the drug to 41 patients (31 with essential hypertension, 5 with renal hypertension, and 6 with malignant hypertension) over an average period of 16 weeks The drug was effective in lowering blood pressure, particularly with the patient in the upright position Addition of a natruretic drug of the thiazide series, singly or with hydralazine, greatly enhanced the hypotensive action of bretylium tosylate Another great advantage of this new drug, apart from its potent hypotensive effect, was the almost complete absence of parasympathetic blocking effect Tolerance to the drug appeared to develop in one patient of the series

On the basis of his brief experience Lewis (*Canad M A J* 82 877, 1960) found bretylium tosylate to be a significant advance in the treatment of hypertension Certain annoying or semidisabling side-effects produced by ganglionic blocking agents were not correspondingly significant when this drug was used Pharmacological effects appeared to be confined to sympathetic nerve interruption within the dosage limits used Subjective muscular weakness was noted in two patients In two others, digestive symptoms of undetermined cause, followed by vomiting and obstipation, occurred after the use of relatively large doses The possible presence of hyperchlorhydria from relative vagal predominance was not investigated, but no serious side-effects were noted in the short period of observation

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The items in these letters are contributed by regular correspondents in the various foreign countries

Metabolite 1 for Rheumatic Disorders—A series of 353 patients who had various rheumatic disorders were treated with metabolite 1 of phenylbutazone (G-27202) Graham (*Canad M A J* 82 1005, 1960) reported that the response was excellent in ankylosing spondylitis and gouty arthritis In osteoarthritis, rheumatoid arthritis, tendinitis, and other miscellaneous rheumatic disorders, the drug was thought to be worth while, but it should be discontinued if there is no relief in 7 to 10 days Most of the complications were minor and transient in nature, and all major reactions subsided promptly on cessation of therapy The danger of toxicity was reduced by close clinical observation and prompt withdrawal of the drug at the first sign of toxic reaction

G-27202 was definitely less irritating to the gastrointestinal tract than the parent drug, phenylbutazone Its therapeutic effectiveness was a little less than that of phenylbutazone, but some patients who failed to respond to phenylbutazone responded to G-27202 and vice versa About 250 complete blood studies made at intervals throughout the treatment period revealed no evidence of a toxic effect on the blood or marrow

Adrenal Cortex in Senility—Five groups of subjects (normal young persons, normal old persons, young persons with functional psychosis, persons with senile dementia, and old schizophrenics), each comprising 5 men and 5 women, were blindfolded for 30 minutes Samples of blood and saliva were taken immediately before, immediately after, and three and one-half hours after blindfolding The sodium-potassium ratio was determined in the saliva and the number of eosinophils was counted in each sample of blood Kral and Grad (*Canad J Psychiat* 5 8, 1960) reported that, prior to blindfolding, young persons with functional psychoses had the highest eosinophil count of all subjects The counts of this group were significantly higher than those of normal old persons

Moreover, differences between the former group and normal young subjects or old persons with senile dementia were of borderline significance In response to blindfolding, normal young subjects showed a significant eosinopenia, as did also the patients with senile dementia, but in the former case the eosinopenia was apparent immediately after blindfolding but not three to four hours later The patients with senile dementia, on the other hand, presented no immediate eosinopenia but showed a significant change three to four hours later The remaining groups showed no significant change in the number of circulating eosinophils in response to blindfolding

In the case of the salivary Na/K ratio the patients with senile dementia and the elderly schizophrenics had significantly higher values than the other groups prior to blindfolding In response to blindfolding, the normal young subjects showed a significant increase in the Na/K ratio immediately after blindfolding, with a return to normal three to four hours later On the other hand, old schizophrenics showed a significant decline immediately after blindfolding, with a persistence of low values three to four hours later All other groups showed no significant change as a result of blindfolding

These studies provided physiological tests for distinguishing senile dementia from schizophrenia in elderly psychotics Also, because of the inverse relationship between the change in the level of the circulating eosinophils and salivary Na/K ratio on the one hand and the change of the level of the sugar- and salt-influencing hormones of the adrenal cortex on the other, it was suggested that elderly schizophrenics react to blindfolding (stress) by an immediate increase in the output of salt-influencing corticoids, while the patients with senile dementia react to the same stress by a delayed increase in the output of sugar-influencing corticoids

DENMARK

Hydroflumethiazid—Eilersen and Berthelsen (*Ugesk laeger*, April 14, 1960) gave hydroflumethiazid to 206 patients for the relief of chronic cardiac decompensation and other ailments, 51 took the drug for 3 to 14 months These 51 patients included 28 who suffered from cardiac decompensation and, of these, 5 were rendered symptom-free, 21 showed some improvement, and in 2 there was no change The dosage found to be suitable for prolonged treatment was 25 mg of hydroflumethiazid twice daily The dosage of the drug could also be doubled, i e, 50 mg twice daily with a daily supplement of 3 Gm of potassium chloride

In view of the risk of hypopotassemia, regular electrolyte determinations should be undertaken at the commencement of the treatment and later every third or fourth month Side-effects included dyspepsia, fatigue, exanthems, and thrombocytopenia with petechiae Hypopotassemia and hypochloremia were also observed The most troublesome side-effects were the exanthems None of the side-effects was serious enough to necessitate discontinuation of the treatment Most of the side-effects occurred early in the course of treatment

Bacteriology of Urine—With the possibility in mind that catheterization of the female bladder may infect it even when a catheter is passed only once, Hjorth and Sjolin (*Ugesk laeger*, April 14, 1960) devised a cultural test by which they hope useful information can be obtained from urine examined directly after it has been passed in the natural way Using a Petri dish with a diameter of 10 cm, they tested 300 such samples of urine The cultural behavior of the urine varied in some cases according as it was already heavily infected or accidentally infected when passed. In 70 cases (23%) the urine was so heavily infected with pathogens that it was evidently the subject of an already existing infection of the urinary tract. In 189 cases (63%) no pathogens were found. In 259 cases (86%) the findings were "significant" in that they indicated whether the organisms found pointed to a preexisting infection or one of accidental, recent date.

Melena from Aspirin.—Since Douthwaite drew attention in 1938 to the frequency with which aspirin provokes hemorrhage of the upper intestinal tract, much confirmatory evidence in support of his views has appeared. Dr. Anne Frolund (*Ugesk. laeger,* April 7, 1960) persuaded 74 healthy subjects to test the drug's effect in this respect after they had dispensed with meat in their diet for five days before beginning to take it. Every day for a month, 1 Gm. of the drug was given twice. The presence of blood in the feces was sought by the benzidine test. After an interval of a month, this investigation was repeated with the same dosage of the drug. All 74 were examined for melena five times. After the first month occult intestinal hemorrhage was demonstrable in about 33% of the persons tested and after the second month in about 50% of them. These investigations suggest that even a healthy intestinal tract may react to aspirin by occult hemorrhage.

Cerebral Palsy.—Dr. E. Hansen (*Ugesk. laeger,* April 21, 1960) collected a series of 2,621 patients who were born between 1925 and 1953, who had cerebral palsy, and who were still alive at the end of December, 1955. In the same period, 199 such patients were born but died before 1955. To these may be added the 513 patients who had been born in the same period and who presented symptomatically allied conditions suggestive of cerebral palsy. Hansen found a male preponderance for which he had no easy explanation. As was to be expected, the marriage rate was low, with 2,511 unmarried, 103 married, and 7 divorced or not traced with regard to marital status. The mean incidence of cerebral palsy per 1,000 births was 1.3 for the whole period. The number of patients per 100,000 population was 132.

Spasticity in some form was found in 78.5% of these patients. The following figures are percentages showing the frequency with which the patients were mentally equipped: normal mentality 47.7, presumably mentally defective 9.4, certainly mentally defective 11, debilitated 9.8, imbecile 10.3, idiot 7, and not classified 4.8. While these figures tally well with those of earlier Scandinavian observers, English and American observers have found a definitely higher oligophrenic rate. Among the 2,621 were 581 or 22.2% suffering from epilepsy. The cerebral palsy rate was definitely higher when the weight at birth was under 2,500 Gm. than when it was above this figure.

EAST AFRICA

Isoniazid Neuropathy and Dermatopathy.—G. L. Money (*J. Trop. Med.* 62:198-202, 1959 and *West African Med. J.* 9:1, 1960) drew attention to the danger of damage to the nervous system in malnourished, tuberculous patients who were taking isoniazid. He reported that in Nigeria severe effects such as psychotic disturbances, optic neuropathy, polyneuropathy, burning feet syndrome, and even convulsions have been observed in patients who received the conventional dosage of 2 to 4 mg. per kilogram of body weight per day. He suggested that isoniazid therapy interferes with the utilization of pyridoxine. From East Africa, W. S. Haynes (*East African Med. J.* 35:171-180, 1958) reported the development of pellagra in six tuberculous patients who were taking small doses of isoniazid. In these patients, the utilization of niacin was interfered with during therapy. Both writers emphasized the importance of supplementing the diet of tuberculous patients in the tropics with a source of the main members of the vitamin B complex, such as yeast.

Iron Deficiency Anemia.—The report of a study group of the World Health Organization (*Report Series* 1959, no. 182, Geneva) showed that iron deficiency anemia is a major public health problem in the tropics. It especially affects such groups as infants and expectant mothers. The incidence is particularly high in Mauritius where 50% of certain groups of people are anemic, and in 90% of these the anemia is caused by a deficiency of iron. Although the usual tropical diet is adequate in iron content, it is abnormally rich in carbohydrate with high phosphate and phytate and low calcium levels. In this way, iron is probably poorly absorbed. Actual loss of iron (as much as 10 mg. a day) may result from the almost universal infestation with hookworm in certain parts of Africa.

Two recent reports from South Africa (P. Lanzkowsky and D. McKenzie: *South African Med. J.* 33:21-24, 1959, and J. Metz and H. Stein: *ibid.* 33:624-627, 1959) emphasize the importance of iron deficiency anemia in the African child. Lanzkowsky and McKenzie estimated the hemoglobin levels of healthy Negro and Bantu (Negroid) children attending local nurseries in Cape Town. They found that between 60 and 70% of both groups were distinctly anemic, and that an inexpensive preparation, such as iron and ammonium citrate in a dose of 1.35 Gm. daily, was an efficient hematinic. More expensive preparations, such as ferrous gluconate and colloidal iron, were equally effective.

Metz and Stein reported on a series of 60 Bantu infants in Johannesburg with a hemoglobin level of less than 10% Gm., MCHC, 30% or lower, and hypochromic erythrocytes present in the blood. All but six of these children were severely malnour ished The authors stressed the importance of nutritional factors in causing the anemia in these infants Only half of the number were breast-fed for as long as three months, and in nearly all instances the diets onto which the child was weaned contained no adequate source of iron Poor absorption of iron in these children was also partly responsible for the anemia, because iron therapy by mouth was unsatisfactory They were able to confirm the report of H C Trowell and M J Simpkiss (*Lancet* 2 265, 1957) from Uganda of the efficacy of iron given intramuscularly in the treatment of the iron deficiency anemia of kwashiorkor

GERMANY

Hepatic Blood Supply—Kummer and Ott of Landshut (*Munch med Wchnschr* 101 2399, 1959) measured hepatic blood supply by the colloidal gold method They injected 30 to 50 μc of Au^{198} into the right brachial vein and took blood samples from a vein of the other arm after 2, 4, 6, 8, and 18 minutes The method gave fairly exact values The fact that 10, or at the most 24, hours after intravenous injection of Au^{198} no trace of the substance was still present in the blood made it possible to make the second examination on the next day At this time the same dose of Au^{198} was preceded by the drug under test Great variations of the clearance constant (k) in both disease and health were found in some subjects, and the limit of k was found to be about 0 10, above which hepatic blood supply can be considered as normal Average values in health were 0 13 to 0 16, in decompensated cirrhosis they were reduced, and in acute hepatitis they ranged from 0 04 to 0 06 Individual clearance was found to be constant

Seventy-seven patients, in some of whom hepatic circulation was severely impaired, were given kallikrein, dehydrocholic acid, and cystein, which did not significantly change the values Thioctic acid gave different results in the 26 patients to whom it was given It effected an improvement in blood supply by more than 10% in 16 patients, by more than 20% in 13 of these, and by 0 to 10% in 9 and the value decreased in 1 patient There was no definite indication of an interrelation between the degree of effect of the drug and the initial value of hepatic circulation and dose The decisive factor in the effect of thioctic acid appeared to be whether the hepatic disease was organic or functional

The greatest increase in circulation was seen in hepatitis and hepatic cirrhosis (usually more than 30%) Patients in whom the increase was between 10 and 30% were those with less marked disorders of the peripheral circulation due to sclerotic, angiitic, or hormonal causes An increase of less than 10% was achieved in health and in patients with cardiac insufficiency who had congestive icterus and in those with mechanical icterus If these observations are confirmed in a larger series, it may be concluded that hepatic circulation is regulated not only in health but also in insufficiency of the right heart and particularly in mechanical icterus, and that measures improving hepatic circulation cannot be expected to effect further improvement Conclusive indications of the duration of the effect of thioctic acid in patients with damage of the liver parenchyma could not be obtained by these studies

Operative Risk in Prostatic Hypertrophy.—H Schneider of Karlsruhe (*Med Welt,* no 3, 1960, p 166) stated that a reliable conservative treatment for hypertrophy of the prostate is not yet available Too large a dose of hormone may favor the development of a prostatic carcinoma Not every patient with hypertrophy of the prostate requires surgery Many patients have only minor complaints, and external irritation can cause sudden acute urinary suppression which can be controlled by a single catheterization The size of the prostate is not always a reliable guide in deciding whether an operation should be performed Isolated hypertrophy of the median bar or sclerosis of the sphincter may severely impair evacuation of the bladder, although they are small in size

The mechanical obstruction may be added to by nervous disturbances with pollakiuria and nocturia which can be controlled by appropriate living habits and administration of male and female sex hormones Patients with genuine adenoma rarely respond to such measures Whenever the condition becomes troublesome, operation should be considered Prior to operation, it is necessary to determine renal function and obtain an intravenous pyelogram In spite of all technical advances, operation on the prostate has remained a major operation Men of advanced age in whom cardiac and circulatory functions are already insufficient are usually affected The condition itself causes, via renal damage, further impairment of circulation and metabolism

Whenever renal concentration capacity has decreased below a specific gravity of 1 015, the risk associated with operation is increased An increase of blood nonprotein nitrogen represents a momentary danger but frequently can be controlled by permanent catheterization

Schneider surveyed a series of 2,650 patients, of whom 1,450 had prostatectomy and 1,200 had transurethral electroresection Total mortality was 2 1% (5 5% among the prostatectomized and 0 3% among the resected) Prostatectomy is therefore the more dangerous operation Most of the deaths were due to pulmonary embolism Anticoagulant prophylaxis is not possible in these patients because of the great danger of bleeding Operation is best performed with the patient under hexobarbital and local anesthesia If these are insufficient, nitrous-oxide and oxygen or, in young men, curare can be used The risk of operation could be diminished further, if the patients would come earlier for operation

INDIA

Corticotherapy in Gynecologic Infections—O J Shah (*J Obst & Gynec India* 10 315 [March] 1960) used corticosteroids along with antibiotics in treating certain gynecologic infections where antibiotics alone had failed or when local inflammatory masses persisted after general toxemia was controlled by antibiotics The addition of corticosteroids helped to control antibiotic-resistant infections and to bring about a quick and complete resolution of inflammatory masses within 8 to 10 days, leaving a painless pelvis Such combined therapy was used in 20 patients with pelvic infection, mostly postabortal and post partum, 24 with mammary infection, and 10 with postoperative abdominal wound infections The antibiotics were started first and corticosteroids given later

Prednisone and prednisolone were selected because of their minimum side-effects and maximum benefits with small doses The average effective dose to control the infection was 15 to 20 mg on the first day, 10 to 15 mg on the second, and 6 to 10 mg daily for five to seven days The drug was then gradually withdrawn by reducing the daily dose to 2 5 mg The favorable response in resistant cases was amazing In patients with mastitis treated with antibiotics, persistence of the local inflammatory reaction after disappearance of the general toxemia, leaving a hard sclerotic mass which did not resolve, spread, or suppurate, was common Antibiotic therapy combined with corticosteroids led to quick remission in all such patients Similar observations were noted in patients with postoperative infective induration in the abdominal wall around an incision, or around a persistent sinus Resolution of these masses occurred within four or five days with combined therapy

Hypnotism in Labor—N V Mody used hypnosis for relief of labor pain in 20 selected patients and obtained encouraging results (*J Obst & Gynec India* 10.348 [March] 1960) Only patients who volunteered and were willing to cooperate were selected for this trial All had vaginal delivery The method of verbal suggestion was used Patients were also trained for autohypnosis so as to be able to hypnotize themselves at the start of labor Antenatal hypnotic sittings were given to every patient, except one, who was hypnotized for the first time during labor Maximum depth of hypnosis was aimed at during the antenatal sittings, the depth varying in different patients according to their susceptibility The number of sittings given to each patient also varied, the average being 7 3 The pain was relieved in all seven primiparas and eight of 13 multiparas No relation was observed between the relief of pain and the number of sittings or depth of hypnosis Failure in unsuccessful cases was found to be due to disturbed condition of mind, excessive fever, loss of confidence, prolongation of labor, operative interference, and postmaturity No patient required more than 100 mg of meperidine In one patient hypnosis was successful even after meperidine had failed Post partum, three episiotomies were sutured under hypnosis

Paracentesis Uteri—E J Sequeira (*J Obst & Gynec India* 10 378 [March] 1960) found abdominal tapping of uterine contents of great help in differentiating hydatid mole from normal pregnancy Paracentesis was performed on 20 patients with a long lumbar puncture needle attached to a syringe The uterine cavity was reached through the abdominal wall under local infiltration anesthesia Aspiration of liquor amnii indicated normal pregnancy while aspiration of blood was considered strongly suggestive of hydatid mole Aspiration of blood would occur in normal pregnancy in case the needle entered one of the placental blood spaces, but pushing it deeper or withdrawing it would lead to aspiration of liquor amnii

All 20 patients were suspected of having a hydatid mole Blood was aspirated from the uterine cavity of 14 patients, and all these were found to have a hydatid mole Liquor amnii was aspirated from the other 6, who later proved to have a normal pregnancy Of the 20 patients 10 were also studied roentgenographically and a rat test was done in addition to tapping in 14 None of the 10 examined roentgenographically showed any fetal parts, although 3 were found to have a normal pregnancy Result of the quantitative rat test was potitive for hydatid mole in 10 of the 14 patients Of these, two were later found to have a normal pregnancy Of the remaining four with a negative result, one had a hydatid mole The aspiration test was thus found to be simpler and more reliable as a diagnostic aid than roentgenography or the rat test

Tropical Eosinophilia—J K G Webb (*Indian J Child Hlth* 9 227 [May] 1960) stated that some workers have suggested the possibility that the mechanism of zoonotic infection by helminths is responsible for tropical eosinophilia in Asia The author's investigation was directed at demonstration of organisms in tissue obtained from patients who had an absolute eosinophil count of over 4,000 per cubic millimeter and who had a positive result of the filarial complement fixation test These patients also showed a therapeutic response to diethyl carbamazine, although the blood gave consistently negative results for microfilariae The tissues examined were from the lung, liver, and lymph nodes Microfilariae were demonstrated in the center of nodules seen in each of these tissues, suggesting direct invasion by the organism as the cause of the lesion in this disease

Lung tissue obtained from three patients with tropical eosinophilia and liver tissue from seven with hepatomegaly associated with tropical eosinophilia was examined by serial sections The normal architecture was preserved in both organs but there were nodules scattered irregularly throughout which showed the presence of microfilariae, complete or in fragments inside an aggregate of eosinophils Lymph node biopsy was performed on 14 children with lymphadenopathy as the presenting symptom In two there was no evidence of pulmonary involvement, but the rest of the 11 had typical findings of tropical eosinophilia These nodes on section also showed eosinophil aggregates and granulomas, with portions of microfilariae Thus, this investigation not only revealed the exact nature of lung lesions in this disease but also showed that similar lesions occurred in other organs The causative role of the parasite was definitely demonstrated by its presence in the center of the nodules The lesions also appeared to be a direct reaction to an invading parasite rather than an allergic reaction to a remotely situated organism

Hydatid Mole—B G Mody (*J Obst & Gynec India* 10 307 [March] 1960) subjected samples of urine from pregnant women to semiquantitative estimations or dilution tests in order to provide information regarding urinary chorionic gonadotropin excretion in patients with hydatid moles before and after evacuation and to determine the validity of a single semiquantitative test As a positive test result indicated an approximate urinary content of 3,000 I U or more of chorionic gonadotropin per liter, positive responses of specimens diluted 1 10 and 1 100 will not contain less than 30,000 and 300,000 I U per liter, respectively When the level falls below 3,000 I U the result of the test is usually negative

To determine whether the excretion of this hormone stops after evacuation of a mole, day-to-day follow-up of patients was undertaken and both qualitative and quantitative estimations were made until a negative reaction was obtained This was possible in only 10 patients A higher incidence was seen in multiparas than in primiparas Of 64 primiparas, 12 gave a history of abortion within the preceding year while in most multiparas the last delivery was at least two years earlier No moles were detected in the first, seventh, eighth, and ninth months of pregnancy The first month was too early to detect the presence of a mole and the last trimester was too late for the mole to continue unevacuated The results of the tests showed that a single dilution test as a means of differentiating normal pregnancy and a hydatid mole was 94% accurate The author believed that positive reactions from highly diluted urines obtained after the peak excretion of chorionic gonadotropin in normal pregnancy might be more reliable Some patients with a mole showed weakly positive or even negative reactions Thus a negative reaction did not exclude the presence of a mole and a normal pregnancy can also give repeatedly negative reactions Semiquantitative dilution tests thus should be interpreted with caution after considering the clinical data

The day-to-day follow-up after evacuation showed that after evacuation reactions would usually become negative after a week If a positive reaction continued beyond seven days, some abnormality should be suspected In patients with retention of chorionic tissue or the onset of malignant changes, the chorionic gonadotropin excretion continued till the tissue was removed or regressed spontaneously One or more temporary negative phases occurred in some patients All the 10 patients in the present series had positive reactions in 1 100 dilution before evacuation The quantitative test result remained positive for an average of 2 6 days and the qualitative for 5 5 days after evacuation The author advised repeated dilution tests every month for six months after removal of a mole to detect metastases before they are manifest clinically Evidence of malignancy after evaluation was found in 12% of the moles

SWEDEN

New Dairy Product—A new tasteless product derived from milk, rich in albumen, and intended for patients with easily upset stomachs, was developed at the food hygiene department of the Royal Veterinary College in Stockholm It is now being produced on a minor scale by Swedish dairies So far the product is sold mainly to hospitals The product, Famos S 67, is a powder with an albumen content of 67% It is made of skim milk from which milk sugar and milk salt have been extracted, and it has no milk characteristics Being tasteless and completely neutral it is well suited as a food additive to speed up the healing of wounds and to help the patient to regain his appetite The World Health Organization is interested in its value as a weapon against famine diseases Since people in many areas of the world are unaccustomed to the taste of milk, it would be of great value if they could be supplied with a neutral albumen product as an alternative to ordinary skim milk powder or dried milk

Venography for Fractures of the Femoral Neck—Sven Dahlgren (*Acta chir scandinav* 117 494-500, 1959) made intraosseous venograms at the same time as the initial treatment of 25 patients with medial fractures of the femoral neck Two important technical details were stressed First, the patient should be nursed in extension for three days prior to the procedure, otherwise the contrast might easily leak into the fracture at the time of the examination Second, the obturator foramen must be included on the film so that a contrast-filled obturator vein can be seen On follow-up all those who did not show contrast-filled vessels leaving the femoral head at the time of the examination subsequently sustained manifestations of necrosis of the femoral head One of nine patients with contrast-filled vessels also developed necrosis The author concluded that venograms made at the same time as the fracture was nailed were of value in assessing the prognosis of fractures of the femoral neck

Nosocomial Urinary Tract Infections —Nosocomial urinary tract infections caused by Proteus and other gram-negative rods were found in 67 of 69 men treated with indwelling catheters, as reported by Carl-Fredrik Liedberg (*Acta chir scandinav* 118 45-52, 1959) In 54 of the 57 patients who were not infected with Proteus on admission, the nosocomial bacterial flora were isolated subsequent to the retention of the catheter In 29 of these, isolation occurred within the first four days of catheter treatment Unquestionable nosocomial urinary tract infection was seen in only 6 of 36 patients not treated with indwelling catheters In regard to modes of infection, micro-organisms can be pushed into the bladder when the catheter is inserted This mode of infection was probably uncommon in the present series Micro-organisms may migrate up to the bladder via the urinary drainage bottle, the lumen of the connecting tube, and the lumen of the catheter An indwelling catheter often causes a slight urethritis Bacteria have been shown to be able to migrate from the urethral orifice to the bladder by way of the exudate that forms between the urethral epithelium and the wall of the catheter These last two modes of spread seemed most likely in the present series since micro-organisms which belong to the nosocomial flora were found in the blankets of patients, and thus a dissemination of the micro-organisms to uninfected patients was possible via the dust and the hands of the personnel No benefit was observed from the prophylactic use of antibiotics

Operative Injury to the Ductus Choledochus —A series of 17 patients with operative injury to the common bile duct were treated by Stig Borgstrom (*Acta chir scandinav* 118 25-31, 1959) Severance of the duct may be overlooked during the primary operation If the intrahepatic biliary tree is not filled out by contrast medium, the possibility of such a lesion should be suspected until the contrary is proved The 17 patients underwent a total of 59 operations The number of operations per patient ranged from two to seven Six patients died as a direct result of the trauma to the ductus choledochus Nine patients have been asymptomatic since their last operation The observation period varied from five months to over nine years End-to-end anastomosis of the ductus choledochus was performed 15 times Only two of the patients were still asymptomatic, 5 and 40 months, respectively, after removal of the ductal drain Generally the symptoms of biliary obstruction appeared within five months of extraction of the drain Transitory absence of symptoms, however, was achieved for as long as four years in one patient in this group

No parallelism was demonstrated between the length of time that the drain was retained (up to six months) and the duration of freedom from symptoms after its removal Hepaticoduodenostomy was performed nine times on eight patients Seven of these patients were rendered asymptomatic, one of them, however, only after an operation for relief of biliary stenosis The observation time of this group ranged from one year and seven months to nine years and three months The author concluded that in hepaticoduodenostomy insertion of a tube through the anastomosis was inadvisable Hepaticojejunostomy and enterostomy were each used only as a last resort in this series and gave poor results Biliary stenosis with retention of the sphincter of Oddi was associated with a greater risk of permanent liver damage than was a well-functioning hepaticoduodenostomy

Angionephrography and Renal Tuberculosis —In order to determine the value of angionephrography in patients with renal tuberculosis 29 such patients were studied by Fritjofsson and Edsman (*Acta chir scandinav* 118 60-71, 1959) After urography and angionephrography plus chemotherapy for varying periods of time, partial nephrectomy was performed on 14 and nephrectomy on 15 patients The roentgenographic changes were correlated with the pathological changes found in the specimens removed at operation The authors concluded that angionephrography was of little or no value in the early diagnosis of renal tuberculosis, but more extensive tuberculous changes in the renal parenchyma could be shown by angionephrography and the more extensive the parenchymal changes were, the more pronounced were the angionephrographic changes Angionephrography often showed the extent of the inflammatory changes more accurately than urography Angionephrography was of special value in revealing the vascularity of the affected areas of the kidney

Knowledge of the extent of the tuberculous changes and the vascularity of the affected areas of the kidney is of great value in estimating the possibility of combating the tuberculous process by chemotherapy Angionephrography can therefore aid in deciding the length of the course of treatment, whether this treatment should be combined with an operation and, if so, the nature of the operation (partial nephrectomy or cavernotomy in patients with limited changes and nephrectomy in those with extensive changes) In patients in whom renal tuberculosis is complicated by hydronephrosis caused by a stricture of the ureter, angionephrography can reveal the condition of the renal parenchyma and thus aid in the choice between nephrectomy and resection of the ureter with reimplantation into the bladder

Contrast Roentgenography in Differential Diagnosis—Bergkvist and Seldinger (*Acta chir scandinav* 118 137-145, 1959) examined two series of patients by contrast roentgenography One series comprised 14 patients with perforated peptic ulcer in whom free abdominal gas was not primarily demonstrated The ulcer niche was roentgenographically visualized in 12 patients and duodenal bulb deformity in the other two Perforation was demonstrated in nine patients In three of the others, the perforation was concealed The second series consisted of 26 patients with acute pancreatitis who were examined within 48 hours of the onset of symptoms, 19 of them within 24 hours Duodenal changes (stagnation of contrast medium and mucosal atypia) suggestive of pancreatitis were roentgenographically observed in 24 patients and in 15 the appearance of the stomach and the duodenum indicated pancreatic swelling Left-sided pleural effusion, with a single exception, was not demonstrated in the first 24 hours of the illness

The two series comprised 40 patients with similar symptoms, difficult differential diagnosis, and dissimilar therapeutic indications who were studied by contrast roentgenography during the acute stage of their diseases The roentgenograms permitted definite diagnosis in 9 (perforation demonstrated) and provided strong support for one diagnosis or the other in 28 (ulcer demonstrated or pancreatitis highly suspected) These figures illustrated the value of contrast roentgenography for differential diagnosis in the acute phase of perforated ulcer and pancreatitis

Surgical Stress and Thyroid Gland—The effect of surgical trauma on the thyroid function in man was studied by estimating the level of protein-bound radioiodine (PBI^{131}) in the serum before and after operation Curt Franksson and co-workers (*Acta chir scandinav* 118 264-269, 1959-1960) made observations on 10 patients and 12 controls The PBI^{131} level showed a marked increase in some patients compared with the controls, indicating increased secretion of thyroid hormone The authors believed that hypothalamic stimulation might influence thyroid function in two ways 1 Via the hypothalamus, an increased secretion of thyroid-stimulating hormone from the pituitary gland could be provoked 2 By the hypothalamus-pituitary-adrenal cortical interactivity an increased secretion of corticosteroids was obtained which inhibited the thyroid function These mechanisms, which counterbalance each other, control the thyroid function in surgical stress It is possible that sometimes the one, sometimes the other, predominates This could explain why both stimulation and depression of thyroid function may be associated with stress

Cancer of the Breast—A series of 50 patients with metastasizing cancer of the breast (32 in stage 2 and 18 in stage 3) were treated with oophorectomy and given 50 mg of cortisone daily by Persson and Risholm (*Acta chir scandinav* 118 217-224, 1959-1960) Stage 2 was defined as regional metastases in the axilla and possibly in the supraclavicular fossa and stage 3 as generalized metastases The results of treatment in stage 2 could not be judged because the observation time was too short The results in stage 3 appeared to be as good as those observed after adrenalectomy or hypophysectomy Remission occurred in more than 50% of the patients and subjective improvement in more than 75% On the assumption that continued experience produces similar results, oophorectomy combined with cortisone therapy is recommended for the routine method for treatment of cancer of the breast in stage 3 The advantages of this method of treatment in comparison with hypophysectomy or adrenalectomy were that it could be undertaken at any hospital and was relatively free of risk The authors believed that all these tumors were under the influence of a complicated hormonal interaction In stage 2 there is good reason for resorting to such measures in combination with radical mastectomy Oophorectomy in combination with cortisone therapy was, in this case, the only form of treatment that seemed suitable

UNITED KINGDOM

Disinfection of Surgeon's Hands—The effects of some of the newer antiseptics in keeping down the organisms of surgeons and nurses hands were investigated by Lowbury and Lilly (*Brit M J* 1 1445, 1960) who counted the viable bacteria emerging through pinholes in surgical rubber gloves after they had been worn for an hour Scrubbing the hands with soap and water for five minutes only halved the bacterial count Besides not being very effective, repeated and prolonged scrubbing can damage and macerate the skin and make it even more susceptible to infection

The authors pointed out, however, that removal of the horny layer makes the skin flora more accessible to antiseptics Using the five minutes routine surgical scrub as a control, they found that viable bacterial counts were reduced to less than 10% by the inclusion of 5 mg of *neomycin* and 5 mg of bacitracin in the glove powder, by a three minute rinse in a 70% alcohol solution alone or one containing 0 5% chlorhexidine, and by using hexachlorophene soap or phisohex for the scrub and for all ablutions during the week before the investigation Phisohex is a combination of 3% hexachlorophene and a cream containing an anionic detergent, Phisoderm Phisohex was superior to hexachlorophene soap, and chlorohexidine in alcohol was somewhat better than alcohol alone The regular use of hexachlorophene soap by nurses in two accident wards and a burns unit resulted in a mean reduction of about 67% in the counts of viable bacteria and Staphylococcus aureus in hand washings All the staphylococci isolated from nurses' hands were highly sensitive to hexachlorophene, which did not produce sensitivity Thus although these new antiseptics may reduce the contamination of Staph aureus through hands, they cannot eliminate the organism entirely

Radioisotope Industry—The Radiochemical Center, part of the United Kingdom Atomic Energy Authority, has been developed at Amersham to meet the demand for radioisotopes at home and abroad in medicine, biochemistry, and industry Here about 230 labeled compounds are prepared These include labeled cortisone, cholesterol, ganglionic blocking drugs, nicotinic acid, amino acids, sex hormones, folic acid, thymidine, and histamine The radioisotopes are sent all over the world, mainly by air Effective screening is needed, and sometimes the containers weigh several tons The short-lived isotopes require rapid transit, but even so those with a half-life of seven days can be sent anywhere by air The cost is based on the radioactivity when received and not when sent

Smoking and Personality—The discovery of a statistical association between lung cancer and smoking has led to the view that a causal relationship exists between them This was criticized by Sir Ronald Fisher on the grounds that other alternative and no less plausible explanations exist He suggested that smoking habits and proneness to lung cancer might be due to some third variable underlying both Innate personality features might determine one's behavior with respect to smoking and also to proneness to lung cancer This aspect of the problem was examined by Eysenck and co-workers (*Brit M J* 1 1456, 1960) By means of questionnaires sent to 21,360 men, both smokers and nonsmokers, they investigated the hypotheses that smokers are more extraverted than nonsmokers, that they are less rigid, and that they are more neurotic than nonsmokers

According to the first hypothesis, smoking habits should be related to extraversion in the sense that the amount smoked would increase with the degree of extraversion This was derived from the well-known characteristic of the extraverted personality to concentrate on objects in the outer world, in contrast, the introvert tends to be occupied with his own thought processes and other internal states According to this hypothesis extraverts would be expected to be heavy consumers not only of tobacco, but also of alcohol, candy, and other pleasure-giving substances The second hypothesis is related to the belief that the rigid puritanic-minded type of person is less likely to indulge in smoking, which like all pleasurable activities might be regarded, consciously or unconsciously, as slightly sinful The third hypothesis suggested that the more emotionally unstable, neurotic type of person would be the heavier smoker because smoking, like other motor and sensory habits, reduces the strength of an aroused emotion For a person of this type tobacco would become a solace

Those questioned were selected at random from urban and rural areas throughout the country and classified according to age, social class, and occupation Smokers were further classified as light, medium, heavy, and smokers of pipes The questions asked were designed to elicit the personality traits as well as the smoking habits The results of the investigation supported the hypothesis that genotypic personality differences are related to smoking habits Smokers were found to be strongly extraverted but no more neurotic than nonsmokers They were slightly less rigid Smokers of pipes were found to be different from smokers of cigarettes from the point of view of personality, the former being the most introverted group studied

Eczema and Soap—In an annotation, the *British Medical Journal* of June 4 comments on a lecture by Dr F R Bettley to the Royal College of Physicians Eczema of the housewife's hands is one of the general practitioner's commonest and most intractable problems In his uncertainty about its true cause he may tentatively accept the patient's assertion that soap and household detergents must be held responsible The dermatologist, with a show of confidence which he will usually admit is grounded on clinical impressions and prejudices rather than on solid experimental evidence, may either support those opinions or partially or completely exonerate the cleansing agents and lay the blame squarely on the patient's psyche

Dr Bettley made a detailed survey of some of the effects of soap on the skin His experimental work suggested that soap can facilitate penetration of the epidermal barrier by its own potentially irritating fatty acids, alkalis, and other substances The incorporation of soap in barrier creams is therefore inadvisable On the other hand, the direct irritancy of soap has probably been exaggerated It is true, however, that dermatitis from soap is uncommon and is manifested as diffuse erythema and chapping It is unlikely that soap is the primary cause of the nummular eczema of housewives' hands The extent to which soap aggravates eczema is difficult to assess It appears to do so in some patients, but the wholesale prohibition of soap in all patients with eczema cannot be justified

Against the weight of evidence tending to exonerate the soaps and detergents as important causes of eczema must be balanced the firmly held convictions of many clinicians There is no doubt that in some patients soap and detergents can initiate or aggravate eczema of the hands, particularly when used in concentrations many times greater than those recommended, but in most cases the unwarranted incrimination of these cleansing agents serves to distract attention from the actual causes and to discourage investigation Eczema is a complex cutaneous reaction determined by the interaction of many factors Metabolic and emotional factors modify the reaction threshold of the skin to external stimuli and potentiate their direct chemical or allergic effects

After eczematous changes are produced, their perpetuation may depend on the continued action of the initiating factors or on secondary infection, inappropriate treatment, or even an autoimmune mechanism Every case of eczema of the hands requires careful individual assessment, and, although true cases of dermatitis caused by soap or detergent undoubtedly occur, the hasty and uncritical application of this diagnosis can lead the physician to give the wrong advice

Anticoagulants and Apoplexy—The value of anticoagulants in the treatment of acute cerebrovascular incidents is still uncertain Thrombosis is undoubtedly one of the causes of apoplexy, and by analogy with the use of these drugs for other occlusive vascular lesions it is reasonable to suppose that they might be of benefit In acute apoplexy the principal difficulty lies in making a correct pathological diagnosis, because the same clinical findings are associated with interruption of the same neural pathways by different processes Previous trials with anticoagulants have failed to distinguish the different types of lesions, their severity, and their duration

Marshall and Shaw (*Lancet* 1 995, 1960) reported a trial with the anticoagulant, phenindione, designed to assess its value in decreasing the immediate mortality of patients with acute cerebrovascular accidents of recent occurance Patients with hemorrhage, rheumatic heart disease, and myocardial infarction were excluded To improve diagnostic accuracy, all patients in the trial were subjected to cerebral angiography There were 26 treated and 25 untreated patients in the series They were all under 70 years of age, and during the three days before hospitalization they had sustained severe and persistent disturbance of brain function thought to be due to an acute cerebrovascular lesion other than hemorrhage, extradural or subdural hematoma, aneurysm, or arteriovenous malformation The diagnosis was based on the history, clinical examination, lumbar puncture, radiography of the skull, and angiography of the appropriate cerebral vessel

In all patients treatment was started within three days of the onset of the condition Survival or failure to survive for six weeks from the start of treatment was the criterion on which results were based The authors concluded that anticoagulants, when used according to the criteria of selection and management of their trial, are of no value in the treatment of acute cerebrovascular accidents They may even be harmful if a cerebral hemorrhage is misdiagnosed, a not unusual occurrence

Rubella in Pregnancy—Gray (*Brit M J* 1 1388, 1960) described the fetal lesions in six cases where pregnancy was terminated because of rubella in the mother The duration of pregnancy at the time of onset of the rubella varied from 14 to 63 days, and the length of the embryo was from 38 to 151 mm Complete serial sections of the embryos were made Gross and histological appearances were compared with those of normal embryos of similar stages of development Three of the embryos had abnormalities in the ears, heart, and eyes, and one may have had a lesion in the lens A 37-day-old embryo measuring 53 mm had a bilateral lesion of the organ of Corti, the basal and middle coils of which were affected The lesion appeared to be a lysis of the cytoplasm of the epithelium, followed by complete disappearance of the cells There was a strong suggestion of a lesion in the lens Another embryo, 7 weeks of age, 151 mm long, had a completely absorbed septum primum of the heart, which would have caused a persistent foramen ovale had the embryo survived The lenses of a 14-day-old embryo were represented by an amorphous mass broken into clumps of various sizes Gray considered that, at the period when the fetus is affected by rubella, it behaves like an infected tissue culture and that when the virus gains admission to embryonic cells it interferes with their metabolism and causes developmental abnormalities

Diseases of Trophoblast—The Royal College of Obstetricians and Gynecologists, with the support of the Pathological Society of Great Britain and Ireland and the Association of Clinical Pathologists, has decided to create a subdivision of its Tumour Registry for Diseases of Trophoblast Material from evident cases of chorioncarcinoma and hydatid mole is wanted, and the registrars would particularly welcome material from borderline cases Clinicians and pathologists are invited to submit clinical data (on forms to be supplied), pathological tissue paraffin blocks, and histological sections

Medical Television.—The British Broadcasting Corporation was accused by Dr. C. D. Stewart of putting dangerous medical rubbish on television. In the *British Medical Journal* he urged the British Medical Association to take action. He mentioned a program in which patients, including some with rheumatoid arthritis, told how they were improved by cortisone. He was shocked that the B. M. A. took no action in restricting the showing of such misleading programs. Educating the public on medical matters is a good thing up to a point, but television programs should be produced by someone who knows the dangers of showing technical data to an untrained audience.

Denationalization of Hospitals Urged.—In his presidential address to the Royal Society of Health Congress, Lord Morrison of Lambeth, pioneer nationalizer and leading member of the 1945 Labor Government which introduced the National Health Service, suggested denationalizing the hospitals. This proposal was made because in the absence of financial competition neither labor nor conservative governments had been able to stem the increasing cost of the health service, and under the present hospital system it is difficult for an aggrieved citizen to obtain redress. The average citizen who might be having some problem regarding his local hospital does not know to whom to complain. He did not vote for those in charge at the last election, and he does not get a chance to vote against them at the next. When the hospitals were under local government he could write to his local councillor and air his grievances.

The present regional boards and management committees believe that no amount of money is too much to spend on their hospitals. The only check on them is made by the minister of health, he is a politician and must face the next election, and if he cuts estimates he loses support. When hospitals were under the local authorities there was healthful competition for money. The hospitals committee competed with the education, housing, and other committees. A public service, however, cannot be run on the basis of letting everybody have all the money they want. Lord Morrison suggested that possibly laboratories and important scientific research affecting health, the consultant service, which is specialized and expensive, supplies, which on a large scale the government can buy more economically, and the teaching hospitals should all remain in government hands.

Steroid Arthropathy.—Another condition, steroid arthropathy of the hip, must be added to the growing list of iatrogenic diseases. Rapid destruction of the femoral head with consequent disorganization of the hip rarely, if ever, occurs in uncomplicated rheumatoid arthritis or osteoarthritis. Sweetnam and co-workers (*Brit. M. J.* 1:1392, 1960) recently observed such destruction of the hip in four patients treated with corticosteroids. The most striking feature of these cases was that the patients were relatively free from pain. Corticosteroids delay progressive radiologic degeneration of joints in the hands and feet of patients with rheumatoid arthritis, but the hip seems to react differently, presumably because of the enormous force transmitted through it.

Two of the four patients had been given corticosteroids for the treatment of rheumatoid arthritis, one for osteoarthritis and one for pemphigus vulgaris. All showed destructive changes in the hip, osteoporosis and fragmentation of the head of the femur, and little or no pain. These changes occurred during periods varying from 15 weeks to 4 years after treatment with corticosteroids was started. The patient with pemphigus was of special interest because there were no lesions of the joints of any description until prednisone was given. The roentgenologic appearances of the hip in three of the patients were indistinguishable from those of a typical neurogenic arthropathy.

The dose of corticosteroid required to produce destructive joint changes varied greatly. In one patient a daily dose of 10 mg. for only 15 weeks was sufficient. The possible damaging effects of corticosteroids on the joints should be more widely recognized. As the number of patients receiving steroids increases, more will undoubtedly be seen in whom arthritic, and even previously normal, hips have crumbled away. Careful observation of patients on large doses or long-term corticosteroid therapy therefore becomes essential.

Advertising and Medical Profession.—The Council of the British Medical Association in its Supplementary Annual Report (*Brit. M. J.*, April 23, 1960) gives its amended views on the present position of advertising. The alterations were largely caused by the impact of the radio and television. Ultimate responsibility in all these matters rests with the person concerned, but practitioners finding themselves in doubt as to a course of action or safeguards necessary are advised to seek guidance from the secretary of the Association. In the opinion of the Council of the Association the word "advertising" in connection with the medical profession must include all those ways by which a person is made publicly known, either by himself or by others without objection on his part, in a manner which can fairly be regarded as for the purpose of obtaining patients or promoting his own professional advantage.

It is generally accepted by the profession that certain customs are so universally practiced that it cannot be said that they are for the person's own advantage, as, for instance, a doorplate with the simple announcement of the doctor's name and qualifications Even this, however, may be abused by undue particularity or elaboration Anonymity should be observed as a general principle by the medical profession Departure from this principle is permissible only when the objective of publicity for a doctor or a group of doctors is apparent, paramount, and justifiable in the interests of the general public, in the interests of the medical profession, or as an essential part of providing authoritative information when necessary for the general public In these circumstances anything that could be construed as advertising of the doctor himself should be incidental and reasonably unavoidable for the attainment of the objective It is conceded that practitioners may properly place their views on medical subjects before the public when they can do so with authority In so doing it behoves each one to avoid methods which could be fairly regarded as for the purpose of obtaining patients or otherwise promoting his own professional advantage It *should also be remembered that there are many* things innocent in themselves which may, by the manner or frequency of their doing, gravely contravene the principle that medical practitioners should not advertise

Discussions in the lay press or in broadcasting on controversial points of medical science and treatment should be avoided by practitioners Such matters are more appropriate for medical journals and for discussion in professional societies The public has a legitimate interest in the advances made in the *science and art of medicine, and it is* advantageous that medical information, discreetly presented, should reach the public through the medium of broadcasting, both for the general instruction of the inquiring layman and for the particular purpose of health education

Medical practitioners who possess the necessary knowledge and talent may properly participate in radio and television programs concerned with medical or semimedical topics The policy of anonymity in all circumstances in broadcasting is no longer tenable, and there is no objection to the announcement of a doctor s name In preliminary announcements and in the programs no laudatory reference should be permitted When the circumstances of the broadcast specifically require it, mention may also be made of the specialty, professorial chair, or office held but otherwise not of medical appointments held A doctor engaged to give a series of talks or appearances is advised to remain anonymous lest the frequency of mention of his name should be considered unethical A medical broadcaster, when broadcasting only to audiences outside his own country, is usually representative of his profession at home, and under such circumstances, even in regular broadcasts, anonymity may be discarded No correspondence should be entered into by a doctor and the lay public on clinical matters arising from his broadcast Great caution is necessary in public discussions on theories and treatment of disease because of the misleading interpretation that may be put on them by an uninformed public which could lead to the subsequent embarrassment of the doctor and the patient

Spiritual Healing —In an editorial, the *British Medical Journal* (May 7, 1960, p 1417), strongly objects to the presence of spiritual healers in hospitals Apparently 235 hospital management committees are prepared to allow them facilities, and only 29 are not A B M A committee stated that there is no evidence that any special type of illness which cannot be cured by medical methods can be cured solely by spiritual healing It is considered that the results achieved by spiritual healing are obtained through the power of suggestion of a powerful personality over the sufferer The committee draws attention to mistakes in diagnosis and in prognosis and to spontaneous cures that may make any form of treatment difficult to evaluate The *B M J* strongly deprecates the fact that certain spiritual healers claim to have cured patients with cancer While it has no objection to the giving of spiritual consolation, advice, or ministration to the followers of a religion, the *B M J* objects to the administration of treatment for diseases by spiritual healers

New Regulations for Poisons —Due to the large number of potentially toxic drugs available for self-medication the list of poisons in the Pharmacy and Poisons Act was greatly extended, *so that the sale* of many such drugs, which were formerly freely available from pharmacies and general stores, is now restricted Changes have also been made in the Poisons Rules When writing a prescription for a scheduled drug, a physician must now give his name and address and that of the patient and must specify, except for preparations in the British National Formulary, the total amount of drug to be supplied, or, in the case of injectable preparations, the amount contained in each ampul and the dose to be taken or administered The prescription must be dated and signed, except on hospital case sheets, on which the doctor s initials are sufficient Prescriptions must be retained by pharmacists for at least two years unless marked to be repeated Included in the scheduled list are the sulfonamides, central nervous system stimulants, and depressants (which includes tranquilizers, some muscle relaxants, and anticonvulsants), the androgenic, anabolic, estrogenic, and thyroid hormones, and the oral antidiabetic drugs

Although the new regulations have brought more drugs under control, antihistaminics have been freed from restriction They must still be obtained from authorized pharmacists and must bear a label stating that they *should be used only under medical* supervision, and, although not obligatory, it is desirable that the pharmacist should point out that the drugs cause drowsiness. The antihistaminics used for the prevention and treatment of motion sickness must bear a label stating that the preparation may cause drowsiness. Two drugs that have caused much trouble resulting from mild addiction are phenmetrazine and bromdiethylacetylurea. Formerly freely obtainable, they can now be purchased only on prescription. The new regulations cannot control drugs that may be marketed in the future. In Britain there is no such body as the United States Food and Drug Administration. It is not incumbent on a manufacturer to satisfy an official authority that a new drug is safe, free from toxic effects, and not likely to cause addiction. Most pharmaceutical firms, however, are reasonably honest in this respect, and if in their opinion a drug is likely to be unsafe and if its sale is not controlled by the pharmacist or the doctor, the Poisons Board is informed. The Pharmaceutical Society from time to time advises pharmacists not to supply certain drugs other than on a physician's prescription or without a warning to the purchaser.

Doctor Fined for Overprescribing.—The Coventry Executive Council imposed a fine on a general practitioner for continued lack of effort to prescribe economically. The Council recommended that $78 be withheld from the doctor's pay by the Ministry of Health, as the doctor's average cost of prescribing per person on his list was 28 cents in excess of the average on the executive council's list and as the frequency with which he prescribed was one and a half times as much. In his defense the doctor claimed that the laws of average should not be applied to therapeutics, that personal consultations and hence the amount of drugs prescribed varied from one practice to another, that wise prescribing, although it might be more than the average for an area, could save patients from spending time in hospital as inpatients or outpatients, and that underprescribing might be as undesirable as overprescribing. He also claimed that he used more new drugs than the average doctor and that he had a number of psychoneurotic patients needing treatment with the more expensive tranquilizers.

The local medical committee concluded that the excessive cost of prescribing arose mainly through the use of excessive quantities of expensive proprietary drugs, corticosteroids, and antibiotics. It was estimated that the doctor had prescribed drugs costing $576 in excess of actual needs.

Steatorrhea.—The standard method of investigating intestinal malabsorption in steatorrhea is a chemical fat balance determination, which requires hospitalization, is time-consuming, and is unpopular as it involves the collection and analysis of feces. Walker and co-workers (*Brit. M. J.* 1:1403, 1960) simplified the diagnosis of malabsorption steatorrhea by giving olive oil labeled with I^{131} and measuring the subsequent blood concentration and urinary excretion of the isotope. The olive oil was iodinated to within about 20% of saturation with I^{131}, and the radioactivity adjusted so that the fat finally contained 20 mc. per 100 Gm. To avoid uptake of the iodine by the thyroid gland, patients were given 0.69 Gm. of potassium iodide three times daily for three days before the test. After an over-night fast, 60 ml. of ordinary olive oil and then a weighed quantity of the diluted radioactive oil were given. The average dose received was 23 μc. After this the patient had a normal breakfast. Venous blood samples were removed into heparinized bottles two, four, six, and nine hours later, and the urine was collected for three or four 24-hour periods. All specimens were assayed for I^{131} by means of a scintillation counter.

The plasma concentration of I^{131} of normal controls showed an increase from zero to a peak of nearly 4% of the administered dose after five hours, falling to just below 3% after nine hours. On the other hand the plasma I^{131} curve of patients with intestinal malabsorption was flat with a peak of 0.6% after six hours. The urine showed a maximum I^{131} level on the first day, with a progressive falling off up to the third day. The excretion from normal subjects in the first 24 hours was about five times that of patients with intestinal malabsorption.

This test permits a diagnosis of steatorrhea within six hours if the concentration of I^{131} in the blood is estimated, or in 24 hours if the urinary excretion is measured. The latter is more accurate as the blood level of I^{131} depends on factors such as gastric emptying and fat utilization, but the 24-hour urinary excretion gives no information on the cause of the steatorrhea. The method depends on an intact liver for the emulsification of the olive oil by bile salts, and is inapplicable in patients with hepatic disease. In normal subjects the 24-hour I^{131} excretion is never less than 30% of the given dose, while in the subjects with intestinal malabsorption it is never greater than 20%. A strong argument for using urinary measurements alone is that the dose of radiation can be greatly reduced, e. g., to 1 μc.

Doctors Pay Increase Approved.—At a special representative meeting of the British Medical Association it was decided by an overwhelming majority to accept the government's recent offer of pay increases. This will give increases of at least $14 a week to family physicians in the National Health Service and greater increases to specialists working in hospitals. More than 50 amendments to the council's recommendations of acceptance were proposed before the decision was reached. Dr. Wand, chairman of the council, warned repeatedly that the attachment of provisos would nullify the offer and they would be back where they started. The Council's proposals were, therefore, accepted without amendment.

MEDICAL FILM REVIEWS

The Cancer Detection Examination 16 mm, black and white, sound showing time 46 minutes Produced in 1960 by Paul Klemtner and Company, Inc Newark, for the American Cancer Society, New Jersey Division Procurable on loan from Eli Lilly and Company, Indianapolis 6

This film was produced from a video tape of a closed-circuit telecast and stresses the point "early diagnosis for good prognosis" It presents Dr Emerson Day, Director of the Strang Cancer Detection Clinic, Memorial Center, New York, who demonstrates the highlights of a routine presymptomatic cancer detection examination The procedures described can easily be followed in the office of the private practitioner According to Dr Day, "It is here [in the office] that the greatest number of potential cancer cases are encountered Indeed, the ultimate success of the entire cancer-control program will depend upon the family physician, since it is to him that the average patient first takes his health problems" To supplement the film, there is a booklet which outlines the complete examination including the necessary procedures that could not be covered in the film presentation This is an excellent film on basic physical diagnosis There is a complete explanation of the signs and symptoms, and the highlights of the examination are touched upon The photographic quality of this video-tape-to-film recording is better than average, and the narration is equally good The picture is recommended for medical students in their course on physical diagnosis It would also be of value to physicians for postgraduate refresher courses

Off the Shelf 16 mm, color sound showing time 30 minutes Produced in 1960 by and procurable on loan from the American Cancer Society, 521 W 57th St New York 19

There are several types of grants in support of scientific research The best known and most common type is the so-called project grant, which is made to support a specific project Applications for such grants are evaluated by committees of experts in the general area with which the project is concerned It usually takes six months or more until an application for a grant is approved and the money made available This film deals with details regarding the operation and purpose of another type of research grant—the so-called institutional grant The important feature of the form of institutional grants which is described in the film is that it is not given to support a specific project but is available to support a new project at short notice This type of grant is meant to facilitate initiation of research which otherwise might be delayed and suffer as a result of it The film is well organized and technically on a high level Photographic production techniques used in this film are satisfactory, and the sound recording is clear and well paced The combination heightens the acceptability of the film s message because of the situation realism, which is often somewhat lacking in the usual film of this type It will be of great interest to those engaged in research needing support as well as to the general public which supports the American Cancer Society

Air Travel and the Cardiopulmonary Patient 16 mm, color, sound, showing time 29 minutes Produced in 1960 by Jack Leib Productions for the United States Air Force, Air Photographic and Charting Service (MATS) Procurable on loan from Air Force Film Library Center, APCS, 8900 S Broadway, St Louis 25

This film is based on a report by the Section of Aviation Medicine of the Committee on Physiologic Therapy Research of the American College of Chest Physicians It is designed to teach practicing physicians a clinical method of evaluating ambulatory patients with respect to their ability to perform commercial air travel Principles of physiology, atmospheric alterations secondary to altitude exposure, and cabin pressurization are explained as well as physiological considerations of various clinical entities No technical errors are noted The photography and music are excellent The subject matter is extremely important and the film is highly recommended for showing to audiences of medical students and physicians

NEW FILM ADDED TO A M A MOTION PICTURE LIBRARY

Coccidioidomycosis 16 mm color sound showing time 30 minutes Prepared in 1960 by Marco Bruschi MD Bakersfield, Calif Procurable on loan (service charge $4) from American Medical Association Motion Picture Library 535 N Dearborn St Chicago 10

This film covers the entire disease entity and places emphasis on the dermatological, roentgenographic, pathological, and laboratory aspects of this illness Geographical distribution patterns of the disease and the epidemiological, medical, and surgical aspects are discussed, numerous patients are presented throughout the film to illustrate these essential points The subject matter is presented extremely well from every angle except that of surgery However, this is not to be considered a detriment to the film since its primary purpose is not, apparently, that of instruction as to the treatment of this disease This is a magnificent film throughout, and, as a technical entity, it is superb The over-all photographic quality of this film is good, although some variations in quality occur because of the incorporation of photographs of patients evidently taken some years prior to the production of this film However, this variation is far less than that usually encountered in situations of this type and does not materially detract from the message in the film The narration is clear and distinct and thereby enables the viewer to follow easily the visual presentation This film has an important message and is recommended for showing to medical students and hospital staff groups and at medical society meetings

BOOK REVIEWS

Cosmetic Surgery Principles and Practice By Samuel Fomon, M D, Director of Plastic Surgery, Manhattan General Hospital, New York Cloth $27 50 Pp 651, with 608 illustrations J B Lippincott Company, E Washington Sq, Philadelphia 5, 4865 Western Ave, Montreal 6, Canada, Pitman Medical Publishing Company, Ltd, 39 Parker St, Kingsway, London, W C 2 1960

A reviewer of any new surgical text always hopes that many new and promising procedures will be described therein Unfortunately, these were not found in the present volume Much of the contents consist of a compilation of previously published works by other authors The title itself is somewhat misleading since only a small portion of the book deals with purely cosmetic surgery However, much of it deals with tumor surgery and the reconstructive procedures for correction of traumatic lesions I fear that if patients carrying surgical insurance benefits apply for allowances, the insurance carriers could use this text as a basis to refuse payments since even the repair of post-traumatic deformities could be considered cosmetic surgery This book does not offer any great contribution to the specialty of general plastic surgery

Paul W Greeley, M D

Einrichtung und Methoden des klinischen Laboratoriums Von Dr med Eberhard Coetze, Professor mit Lehrstuhl fur Pathologische Physiologie der Freidrich-Schiller-Universitat, Jena Cloth 21 90 marks Pp 246, with 69 illustrations VEB Gustav Fischer Verlag, Villengang 2, Jena, East Germany, 1959

This is a practical manual to be used for the routine performance of what we call clinical microscopy and some qualitative and most quantitative chemical tests It is meant to meet the increasing demand for quantitative methods and especially for micromethods It emphasizes economy in materials to be used, including blood, reagents, time, and labor It describes in detail the equipment of a small but efficient clinical laboratory The six pages devoted to this subject are worth reading, especially, by those who are planning a new laboratory Such questions as one large room versus several small rooms, location of work benches, daylight versus artificial light, floor covering, exhausts, prevention of accidents, etc, are discussed Equally valuable is the section on washing glassware The balance of the first introductory chapter deals with instrumentation and general methodology

Part 2 is devoted to the clinical microscopy of urine, stomach contents, feces, spinal fluid, pleural fluid, ascitic fluid, and blood, all of it on 40 pages Only the barest essentials are covered The third part deals with quantitative chemical procedures This section is the most up-to-date Microbiology is not included

The use of the book presupposes good theoretical background and training on the part of the technologist and close supervision by the clinical pathologist The book contains much useful information critically selected and economically presented The paper and print are excellent

I Davidsohn, M D

Physiology of the Retina and the Visual Pathway By G S Brindley, M A, M D, Lecturer in Physiology in University of Cambridge, Cambridge Monographs of Physiological Society, number 6 Editors H Barcroft, L E Bayliss, A L Hodgkin Cloth $7 50 Pp 298, with illustrations Williams & Wilkins Company, 428 E Preston St, Baltimore 2, Edward Arnold (Publishers) Ltd, 41 Maddox St, London, W 1, England, 1960

Light energy is transformed into sight energy largely by complex enzymatic reactions primarily involving the retinal receptors, a group of biochemicals, and a complex coding mechanism in the visual pathways and centers Three dimensional light waves ranging from about 550 to 750 μ in length, with a speed of 186,000 miles per second, after passing through the transparent ocular media strike the posterior retinal layers where they are transformed into sight energy, basically a form of electric energy having a much slower speed These electrical waves which are potentially information, are coded in the occipital visual, motor, and association centers, the frontal sensory and motor centers, external geniculate, anterior quadrigemina, pons, and ganglia These are connected by nerve fibers which are essentially electric wires Especially the technical phases are clearly and thoroughly discussed by the author

In retinal photochemistry the principle known enzymes are cholinesterase, lactodehydrogenase, and chymotrypsin The chemicals include carotene, indicator yellow, iodopsin, pentoneucleic acid, retinene, and rhodopsin Rod vision is closely associated with rhodopsin Cone vision is more complex and not as well understood The electrical retinal activity varies in different animals and in different parts of the retina and visual pathways

The author classifies sensory visual experiments into objective and subjective which latter he divides into those in which identity or nonidentity can be experimentally demonstrated by two senses, and those in which they cannot In some instances these are interchangeable Color vision is primarily de- termined by the length of the luminous energy waves blue violet, 550 μ, green, 650 μ, and red, 750 μ In the visual mechanism, these are accurately coded, making possible color discrimination, luminosity, and saturation Color abnormalities which include monochromates, dichromates, and anomolous trichromates are briefly discussed

The especially well-organized table of contents reflects the author's understanding and orderly presentation The extensive bibliography requires 40 pages Although primarily technical, this volume should be of interest to ophthalmologists who desire a better understanding of present and past concepts of the mechanics and chemistry of vision

Charles A Bahn, M D

Fundamental Techniques of Plastic Surgery and Their Surgical Applications By Ian A McGregor, M B , F R C S , F R F P S Foreword by C F W Illingworth, C B.E , M D , Ch M , Regius Professor of Surgery, University of Glasgow, Glasgow Cloth $7 Pp 244, with illustrations Williams & Wilkins Company, 428 E Preston St , Baltimore 2 E & S Livingstone, Ltd , 16 & 17 Teviot Pl , Edinburgh 1 Scotland, 1960

This book is largely concerned with techniques of soft tissue repair It is the author's intention to supply guidance to the surgeon who must apply the methods of plastic surgery to the many problems encountered in any surgical practice He does this by dividing the book into a section of basic techniques followed by a section on the application of these to situations likely to be encountered The procedures described are those the author prefers The material is presented in a clear and simple manner and is well organized and adequately illustrated This book is not intended for the trained plastic surgeon The surgeon in training or engaged in the practice of any other field of surgery should find much here that can be useful in the management of his everyday problems In the preface the author states clearly what he is attempting to do In the text he ably accomplishes his aim

Louis T Byars, M D

The Plasma Proteins Volume I Isolation, Characterization, and Function Edited by Frank W Putnam Cloth $12 50 Pp 420, with illustrations Academic Press, Inc 111 Fifth Ave , New York 3 Academic Press, Inc (London), Ltd , 17 Old Queen St , London, S W 1, England 1960

The scientific study of blood proteins began in the 1830 s During the 19th century the progress was slow, mainly because of the crude methods of analysis The great advances in our knowledge of plasma proteins in recent years are due to the introduction of physical chemical methods such as moving boundary electrophoresis, paper electrophoresis, ultracentrifugation, chromatography, agar diffusion techniques, and fractionation procedures such as ethanol precipitation The brief introduction defines the subject, reviews its history, and attempts to anticipate future developments The precipitation methods, electrophoresis, ultracentrifugation, chromatography, molecular parameters of purified plasma proteins, albumin, gamma globulin and antibodies, macroglobulins, glycoproteins, and metal-binding plasma proteins are the subjects treated in the remaining chapters The 11 authors are outstanding biochemists from this country and abroad Each chapter has a well-chosen up-to-date list of references

Monographs on plasma proteins that have been published in other languages were usually concerned with use of a particular technique This is the first complete book on the subject which treats broadly, collectively, and exhaustively the many types and functions of plasma proteins The presentation is up-to-date The author index and the subject index are well organized This book should be of interest to biologists and students of disease as well as biochemists The publication of volume 2 dealing with biosynthesis, metabolism, and alterations of plasma proteins in disease is eagerly awaited

I Davidsohn, M D

Progress in the Biological Sciences in Relation to Dermatology Edited by Arthur Rook, M D , M R C P Cloth $15 Pp 480 with illustrations Cambridge University Press Bentley House, 200 Euston Rd , London, N W 1, England American branch, 32 E 57th St , New York 22, 1960

This volume contains papers presented at a course given at Cambridge University to provide physicians in clinical practice an account of fundamental research of particular interest to them The editor has selected a formidable array of topics and grouped them under the headings the melanocyte and melanogenesis, cutaneous innervation, histochemical investigation of the skin, bacteriology and mycology, psychophysiological mechanisms, comparative medicine, immunology, inflammation, carcinogenesis, radiation of the skin, and pharmacology

A few of the writers present their subjects with little direction towards the skin and dermatology—as if the skin were an organ floating in outer space and yet to be discovered by them An example of this is an article dealing with the mode of action of tranquilizing drugs, in which, the effect of these drugs on itching, the major dermatological symptom, is not once mentioned One author, a well-known immunologist, starts his chapter with the statement "I wish to admit freely that my interest in the skin as an organ was really aroused, for the first time, when I was asked to give this talk " This admission may come as a shock to those who have been taught that the skin is a most important organ from the immunological viewpoint

Most of the articles, however, are excellent and meet high scientific standards They are written clearly enough to be useful and stimulating for the practitioner and provide him with insight into both newer thinking and techniques in the biological sciences

Rudolf L Baer M D

QUESTIONS AND ANSWERS

UTERINE CONTRACTIONS

To the Editor.—*In studying movements of the abdominal wall transmitted by uterine contractions during labor and the psychological factors which influence them, a tokodynamometer with strain gauge transducers was used. These receptors proved to be cumbersome to the patients, however, and distracted them. I would like to use a telemetering method similar to the minute radio transmitter which is swallowed to study the movements and variations of pressure of the stomach. How could such an apparatus be constructed?*

M.D., New York.

Answer.—The idea of telemetering intrauterine activity has not been tried in observations in human beings or animals. It is entirely possible, with transistorized and even printed circuits, that this could be done. Telemetering of uterine blood flow in sheep has been done by Assali and associates (*Am. J. Obst. & Gynec.* 79:86 [Jan.] 1960). The problem is one of deciding what type of sensing device to use. The three parameters of uterine function available for recording are (1) uterine shape, position, or both, (2) uterine force (external local pressures or internal amniotic or extra-amenbranous pressures) and (3) electromyographic activity.

Each of these techniques measures one aspect of uterine behavior; no one of them tells much about the other two. Even in measuring uterine forces, external and internal tocography measure different things. These are defined in "Clinical Measurement of Uterine Forces" by Reynolds, Harris, and Kaiser (Springfield, Ill., Charles C Thomas, Publisher, 1954).

Measurement of "uterine profile" changes was attempted by Fenning and co-authors (*Am. J. Obst. & Gynec.* 38:670 [Nov.] 1939), using photoelectric means. Had the method been convenient and of great value, it probably would have been much used since that time. Electrohysterography has been dealt with recently and extensively by Larks in "Electrohysterography" (Springfield, Ill., Charles C Thomas, Publisher, 1960). While the technique is tricky and evaluation of data difficult, the approach might lend itself to telemetering. Uterine pressures are measured by use of strain gauges (resistance or reluctance types) applied to the abdomen, or by catheter to the amniotic sac. Extensive use of the external strain gauge tokodynamometer shows it to be workable, not too heavy, and easy to master. It requires a cooperative patient who will lie on her back. About 67% of women in labor and virtually all women not in labor will cooperate.

The sensing device must transmit the uterine pressures (internal or local external force) with the strain gauge. The bonded resistance strain gauge (Baldwin Locomotive Co., SR-4) has not been tried but might be used. The unbonded strain gauge (Statham) is the kind used in the tokodynamometer. The reluctance (electromagnetic) gauge was recently reported as successful for recording uterine contraction by Suda (*J. Jap. Obst. Gyn. Soc.* 3:342 [Oct.] 1956). This unit has about the same bulk and weight as the bonded gauge. It appears that if compactness is desired, an SR-4 type of gauge might be used, although this presents numerous technical problems that an electronic expert might overcome.

VACCINIA

To the Editor.—*A 16-year-old girl had severe generalized vaccinia after smallpox vaccination in infancy. There was no eczema or skin rash at any time. Is it safe to revaccinate her? If abstention is desirable, would colleges or travel authorities accept a statement to that effect in lieu of vaccination?*

M.D., New York.

Answer.—A review of the literature on vaccinia and consultation with some authorities in this area have failed to reveal recorded data on the success or danger of smallpox vaccination after generalized vaccinia. It would appear that simple follow-up studies of patients who have had vaccinia have not been made, or if such observations have been made, they are not recorded.

On the other hand, it would seem almost certain that the situation described has occurred previously, and that revaccination has been accomplished without incident. A person who contracted generalized vaccinia in infancy would not remember the event and might well be revaccinated at school entry, before foreign travel, or in fulfilling military obligations. If there were significant hazard in this event, it would almost certainly have been brought to the attention of the medical profession. The military services have had no reason to be concerned with the history of vaccinia in their recruits. Although this argument will not substitute for recorded experience, it gives support to a decision to revaccinate such a person while he is under strict medical observation.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

If it were decided to await further documentation, a statement of the reasons for nonvaccination would probably suffice for college entrance requirement For reentry of a United States citizen to this country, the Public Health Service recommends that any statement relating to the contraindications to vaccinations accompany the traveler This statement will be taken into account by the quarantine officer at the port of reentry, and his decision whether to place the subject under surveillance will depend on his judgment concerning the exposure to smallpox which that person may have experienced Although regulations in other countries differ, it is reasonable to anticipate a similar approach to the problem

It is hoped that your inquiry will stimulate interest in recording observations on revaccination after vaccinia, and that these will be published

INFANTILE CORTICAL HYPEROSTOSIS

To THE EDITOR —*A three-month-old girl has a palpable and visible enlargement of the jaws Periosteal thickening of bone structure was demonstrated by roentgenogram There was no osseous involvement elsewhere On several occasions the white blood cell count was 21,000 per cubic millimeter with a preponderance of lymphocytes (85%) The serum calcium level was 9 8 mg%, phosphorus 7 5 mg%, alkaline phosphatase 22 8 King-Armstrong units, and sedimentation rate 36 mm per hour The urine contained 8 to 10 red blood cells and 15 to 20 white blood cells per high-power field The temperature was normal The child's development appeared to be normal This appeared to be a case of infantile cortical hyperostosis What other investigative study need be done? If the diagnosis is correct, what is the treatment?*

M D , California

ANSWER —From the available data, your assumption that this is a case of infantile cortical hyperostosis seems correct The mandibular enlargement is due to both the underlying hyperostosis and the adjacent soft tissue swelling and edema This is apparently a case of monostotic involvement, whereas the disease frequently involves all the tubular bones of the skeleton as well as the flat bones, including the scapulae and the parietal and frontal bones of the skull Elevations of the serum alkaline phosphatase level and sedimentation rate are characteristic

Since the etiology and pathogenesis of the disease are unknown, there is no specific treatment Fortunately, the disease is self-limited but usually runs a course of three to twelve months, after which the swelling subsides and the skeleton assumes a normal roentgenographic appearance Occasional instances of the disease are known to run a course of two to two and one-half years, with recurrent remissions and exacerbations There is no recorded instance of permanent deformity or disability after such a course Since Caffey's original description (*Am J Roentgenol* 54 1 [July] 1945), many references to this disease have appeared in the literature

ADRENOCHROME

To THE EDITOR —*Will you please evaluate for me the use of adrenochrome monosemicarbazone sodium salicylate complex (Adrenosem) for postoperative tonsillar and adenoidal bleeding?*

Byron N Lingeman, M D , Crawfordsville, Ind

ANSWER —Adrenochrome monosemicarbazone sodium salicylate complex is the subject of two articles Roskam and Derouaux (*Arch internat pharmacodyn* 69 142, 348, 1943) claimed it had hemostatic properties, and Parrott and Cotereau (*Compt rend Soc de biol* 139 902, 1945 and *Chem Abstr* 40 6654, 1946) reported that 0 5 mg of adrenochrome, when given to guinea pigs, produced an increase in capillary resistance which persisted for several days These reports apparently still await confirmation The confirmation of any possible beneficial action in the cure of postoperative tonsillar and adenoidal bleeding is difficult because of the transient nature of such hemorrhage and the difficulty of establishing an end-point at which the hemorrhage is controlled The use of this material in a double-blind study as a preventive of bleeding would be feasible, but thus far such studies have not been undertaken Since adrenochrome was introduced after the Food and Drug Act of 1938, it can be stated that the material is probably nontoxic We cannot be certain, however, of its therapeutic effect

UNEXPLAINED LEUKOCYTOSIS

To THE EDITOR —*In the course of examining yearly about 400 men and women employees of a bank averaging 40 years in age, I have observed an unexplained leukocytosis in about 17% of them The differential count, however, is always essentially normal The leukocyte count is between 10,000 and 13,000 per cubic millimeter I have also noted that about 50% of those showing a leukocytosis on one examination have also shown it on previous and subsequent examinations There is no history or evidence of infection in any of these employees I have also noted that about 9% of these persons show a relative lymphocytosis, for which I have no explanation Can you give me an explanation for these findings?*

B L Hardin Jr , M D , Washington, D C

ANSWER —Although the normal leukocyte count in the adult is generally stated to be between 5,000 and 10,000 per cubic millimeter, it should be noted that in the careful study of Garrey and Bryan (*Physiol Rev* 15 597 [Oct] 1935) 11% of apparently normal persons were found to have counts above 10,000. Other studies have confirmed these data. Thus, although the range is 5,000 to 10,000 in most normal persons, any large group will include a certain proportion with counts above these levels. Admittedly, however, the 17% figure cited in the inquiry seems high. It should be noted that physiological variations in the leukocyte count may occur as, for example, with excitement and other circumstances which may be associated with a health examination (Wintrobe: Clinical Hematology, Philadelphia, Lea & Febiger, ed. 4, 1956, pp. 226-228). Under conditions of physiological stress, leukocytes may be swept into the circulating blood stream from dilated capillary beds where they have been lying dormant loosely attached to the endothelial walls. The marginal pool may be as great as the circulating pool of leukocytes. It may be expected that some variation in the normal lymphocyte count would be seen. There is no doubt, however, that a person in whom an abnormal leukocyte count is found deserves careful examination to rule out any underlying disease.

MALMSTRÖM VACUUM EXTRACTOR

To the Editor:—*I have read about use of the Malmstrom vacuum extractor for the delivery of babies. It apparently is less traumatic to both infant and mother than regular forceps and (according to the literature) causes no brain injury if applied over a fontanelle. I want to use one instead of low or mid forceps. I also would like your opinion of the extractors that can be used with a placenta previa and other complications of delivery.*

I. S. Meyer, M.D., Decatur, Ala.

Answer.—The present-day model of Malmström's vacuum extractor apparently is used widely in Europe; in fact, in several European clinics it has completely replaced the classic obstetric forceps. The Kings County Hospital, New York, has had experience with it. Its use has been restricted solely to effecting delivery. The vacuum extractor has not been used to stimulate or enhance labor, as has been suggested by several European investigators.

Its use has entailed little if any maternal trauma and from the standpoint of maternal well-being, it is believed that the vacuum extractor will prove to be safer than regular obstetric forceps. Opinion regarding the effect of its use on infants, however, must be held somewhat in reserve. The series observed is neither large enough nor has the infant follow-up been long enough to justify a definite opinion. None of the babies delivered with the vacuum extractor have manifested any immediate significant untoward results. We have had no experience with its use in placenta previa, and at present do not plan to acquire any. At the moment it appears as if the vacuum extractor's prime function will be to bridge the gap between an otherwise difficult forceps operation which should not be undertaken, and cesarean section. In any event, preliminary results have been favorable enough to warrant further clinical trial.

POLIOMYELITIS VACCINATION

To the Editor:—*Poliomyelitis vaccination is now being advocated for all persons under 40 years of age. Since there is no longer any shortage of the vaccine why limit the coverage? I read that in Texas 25% of all paralytic cases in 1958 were in adults. Another report stated that many paralytic cases occurred in persons over 70 years of age. Regardless of statistics, why not advocate that everyone be vaccinated?*

Lyman Crossman, M.D., Detroit, Mich.

Answer.—There is no reason to limit the use of poliomyelitis vaccination to any age group. There is, however, a greater likelihood that persons in the older age groups have had frequent contact with the poliovirus and have already developed their own protective antibodies.

GEOGRAPHICAL FACTORS OF DISEASE

To the Editor:—*Is it true that the eastern part of the United States has the highest alcoholic and suicide rate? Does city living cause more people to have coronary heart disease and peptic ulcers than a rural way of life?*

M.D., Illinois.

Answer.—In his classic study "Recent Trends in Alcoholism and in Alcohol Consumption" (*Quart. J. Stud. Alcohol* 8:1 [June] 1947) Jellinek reported the Pacific region (Washington, Oregon, and California) to have the highest rate of alcoholism, i. e., 5,697 per 100,000, with the Middle Atlantic states second, i. e., 4,675 per 100,000, the North East third with 4,621 per 100,000, and the Eastern North Central states fourth with 4,157 per 100,000. Keller and Efron, updating these data in "Alcoholism in the Big Cities of the U. S." (*Quart. J. Stud. Alcohol* 17:63 [March] 1956), generally confirm these earlier findings.

The data on suicide rates, even as estimates, are not precise enough to project regional differences. In general, it may be stated that urban rates of suicide are far higher than rural rates and that there seems to be a consistent increase in incidence in relation to the increase in size of cities. While it is not sound to derive suicide rates solely from medical examiners' reports, a review of such data suggests that the rates for cities of comparable sizes are about the same. In San Francisco, for example, suicide ranks between the seventh and eighth cause of death, which is similar to the rate for New York City

The anonymity of the city, the attenuation of the binding forces of family, religious, and recreational systems, and accelerated pace of living all impinge not only on alcoholism and suicide rates but also on the variety of psychosomatic complaints whose incidence appears to be consistently higher in concentrations of vertical living

ANTIBIOTICS FOR PERITONITIS

To the Editor —*What is the present thought on the injection of antibiotic solutions into the peritoneal cavity in the presence of gross contamination by bowel contents?*

Robert B N Newell, M D, Rock Island, Ill

Answer —Previously, it was common practice to leave antimicrobial substances in the peritoneal cavity at the time of operation when contamination was present This procedure has been largely abandoned, because the dose is uncertain and dire consequences, such as respiratory depression, might ensue from rapid absorption of the antibiotic It is preferable to give antibiotics parenterally after operation, which allows one to control the dose and the rate of absorption An acceptable regimen is to give 400,000 units of penicillin and 0 5 Gm of streptomycin sulfate twice daily for four or five days after operation, but some other antibiotic may be used, especially if tests for sensitivity have been made

PTYALISM AND PREGNANCY

To the Editor —*I recently delivered a multipara who was plagued during all her pregnancies with ptyalism She recently had her first menstrual period after her last pregnancy, and the ptyalism recurred only during the flow and then stopped spontaneously She has been given many autonomic blocking agents, including large doses of atropine, for this annoying symptom with little relief, and what relief she obtains from it is of short duration She is a tense, neurotic person What treatment is indicated?*

M D, Iowa

Answer —Excessive salivation is rather rare and occurs mostly in pregnancy First, it should be distinguished from gastric regurgitation, by alkalinity of the secretion or absence of acid, presence of amylase, absence of pepsin, and presence of mucin Although one dislikes to put the tag 'psychogenic" on this condition, little is known about its cause One would think that atropine would work well, but it often does not I would use antihistamines, especially those with the greatest sedative action and the long-acting ones If the patient is not depressed, I would give her meprobamate three or four times a day, and if she is depressed Edrisal, which combines amphetamine with aspirin and acetophenetidin I would, in addition, try to work out the psychological problem and put the patient on a high-protein, low-carbohydrate, low-salt diet to decrease the need for salivation Fluids, preferably water, should be given to offset the loss by salivation One of the newer chloride-eliminating drugs, such as chlorothiazide, might also be tried I have never seen this condition occur during the menstrual flow, but I would be inclined to believe that this patient might be on a diet too high in salt and chlorothiazide would tend to correct this, as it does most of the premenstrual symptoms

CHEYNE-STOKES BREATHING AND PREGNANCY

To the Editor —*What is the significance of Cheyne-Stokes breathing in a healthy, 30-year-old woman who is in her sixth month of pregnancy? This type of respiration occurs only during sleep and began in the first trimester of her pregnancy The patient complains that at times she is unable to catch her breath while asleep and then awakens There are no other complaints and physical examination reveals no abnormalities*

M D, New York

Answer —This type of respiratory activity is not a recognized complication of pregnancy This patient may have an unrecognized mitral stenosis that has never given her any trouble in the past and therefore she may be having nocturnal cardiac dyspnea Another possibility is that there is some type of central nervous system disorder, such as a brain tumor, that gives symptoms only while the patient is lying down Some type of hysteria must also be considered The difficulty in breathing may be secondary to some dream sequence Repeated thorough physical and neurological examinations should be performed to determine if any organic cardiovascular or neurological disease is causing the abnormal respirations while the patient sleeps

HODGKIN'S DISEASE AND PREGNANCY

To the Editor —*A 27-year-old gravida 1, para 1, who has a history of Hodgkin's disease of seven years' duration, is contemplating another pregnancy The tumor was mediastinal and was treated with radiation, with no recurrences of symptoms or signs Will future pregnancies cause such a recurrence?*

C Richard Nixon, M D, Blackfoot, Idaho

Answer —It must be remembered that Hodgkin's disease is variable in its development First the diagnosis should be confirmed by biopsy Next, if remissions produced by radiation are long lasting, it can be assumed to be a mild case In general, most authorities believe that pregnancy is not especially good for any patient with a malignant tumor If this patient should conceive and have a relapse during the period of gestation, how would one treat the disease in the presence of the pregnancy? Probably more important, as far as her children are concerned, is the patient's chance of survival and her life expectancy in years More important than anything is her emotional reaction If she is truly anxious to have another baby and is not really aware of having a smouldering malignancy, her wishes probably should be granted

Except for the limitations mentioned above which are partially theoretical a pregnancy probably would not cause much harm I have one patient in whom Hodgkin's disease was diagnosed at the age of 20 years, who also had one child I operated on her when she was 36 years of age for an ectopic pregnancy, at which time she had no palpable abdominal glands She had obtained good remission with repeated courses of x-ray, but died at the age of 40, or 20 years after diagnosis

TRANSMISSION OF IVY POISONING

To the Editor —*A maternity patient contracted dermatitis venenata due to poison ivy about 10 days prior to delivery and at no time had more than three or four areas of skin, each about 1 by 2 or 3 cm, involved with typical vesicles This responded to local therapy, so that the lesions which were on the hand and legs were dry at the time of delivery There was no evidence of secondary infection Should the patient be allowed to breast-feed the baby? Should she be permitted to hold the baby and to feed the baby its bottle? Is there any danger that other babies in the nursery or nursing personnel might contract a dermatitis from the mother or the baby? Should any special precautions be observed in preventing contact between the baby and the mother's lesions? Can poison ivy ever be spread from one person to others through contact with exudate from weeping lesions or from vesicles?*

Rudolph C Gering, M D, Trenton, N J

Answer —There is no reason why a patient with poison ivy dermatitis should not hold and breast-feed her baby or feed the baby its bottle without any special precautions The lesions of poison ivy dermatitis and the vesicle fluid or oozing material from such lesions do not contain the allergenic materials of poison ivy and therefore cannot be the source of dermatitis for the patient or for other persons who are allergic to poison ivy The only way the patient could contaminate herself (and theoretically others) with ivy poison present on the skin is within minutes, or at the most a few hours, after exposure to the plant As a rule, this is long before she has become aware that she is the victim of such a dermatitis

THE HIPPOCRATIC OATH

To the Editor —*I have had a discussion with a colleague about the "Hippocratic Oath" I cannot recall ever taking the oath He, in turn, said he was required to take the oath What is the present status of the Hippocratic Oath?*

Nathan Chaset, M D, Providence, R I

Answer —I am unable to find literary information which will answer this question It was necessary to consult recent graduates, medical deans, and foreign physicians working in a large medical center The following reports are considered trustworthy

1 At Harvard on class day, a meeting of the class and friends and relatives, the oath was read and repeated by the graduating doctors (May 30, 1959) 2 Five graduates of Catholic medical schools state that a modified oath was given prior to graduation 3 The deans of five midwestern medical schools say that the oath has no official status or use 4 The oath is reported to be part of the ritual of two professional fraternities 5 Graduates (aged 30 to 50 years) of 16 medical schools report that the oath was never offered to them 6 Four graduates of Lithuanian schools report that, prior to the Soviet occupation, the oath in an altered form was taken in a grave atmosphere and that the graduate also signed the oath 7 Six graduates of as many schools in Germany, Italy, France, and Sweden report that no oath was required of them

It is evident that a study of current practice would require the circulation of a questionnaire to the various medical schools I have been informed that some talk about the revival of this classical practice was prompted by alarm about the alleged slump in ethical acceptances The complete Oath can be read in the Encyclopedia Britannica, where it is indexed under "Hippocrates"

DISK OXYGENATOR

To the Editor —*How long has the disk oxygenator been perfected for clinical use? About how many units are in use in the United States? What was the generally accepted death rate prior to January 1960 for closure of patent ventricular septal defects with the open heart operation if the disk oxygenator was used?* *M D South Carolina*

Answer —The disk oxygenator was developed in Sweden by Bjork in 1948 It was modified by Kay and Cross in the United States in 1956 Since then it has been used extensively, with only minor modifications While not perfect, it is an excellent and reliable instrument There are probably 50 units currently used in clinical work, and many more in experimental laboratories, in the United States

The death rate for closure of ventricular septal defects depends on such factors as age of the patient, size of shunt, the presence or absence of pulmonary hypertension, congestive failure, and associated anomalies, as in the tetralogy of Fallot These are the factors influencing the death rate rather than the type of oxygenator used

In infants under 2 years of age, and in patients with a balanced shunt, the mortality may be 40% or higher In the most favorable group of patients, aged 5 to 15 years, without complicating factors, it may be as low as 5% A general death rate of 12 to 15% is quoted from several centers

SEAT BELTS AND PREGNANCY

To the Editor —*A woman, seven months pregnant, was in an automobile accident in which she received some fractures and several lacerations of her face There was no interference with the pregnancy The statement was made that, had she been wearing a seat belt, she would have been less seriously injured If, however, she had been wearing such a belt, would there have been an increased danger to the pregnancy?*

M A Shillington, M D, Fort Lauderdale, Fla

Answer —A properly placed seat belt would have kept the woman in her seat Additional information on the nature and causation of the injuries would be necessary to judge whether the seat belt might have prevented the actual fractures and lacerations

The Industrial Medical Association Committee on Standards for Motor Vehicle Drivers has no statistical information on interference with pregnancy but believes that a properly placed seat belt would anchor the pelvis and not cause pressure on the abdomen In other words, there is no reason to believe that the use of a belt would interfere with an otherwise normal pregnancy

DRUG-INDUCED IMPOTENCE?

To the Editor —*In the past a few male patients have complained that while taking amphetamine, amphetamine-like compounds, dextro propoxyphene hydrochloride, or ethoheptazine citrate they have become impotent Is this an unpublicized side-effect of these drugs?*

M D, California

Answer —Search of the literature fails to reveal any reference to impotence after the use of the newer nonaddicting analgesics such as dextro propoxyphene hydrochloride and ethoheptazine citrate The amphetamines, however, are reported to normalize sexual impulses in disturbed patients, relieving sexual tensions in certain behavior problems and psychopathic states and stimulating libido in depressive states

Reference

Leake, C D Amphetamines Their Actions and Uses, Springfield, Ill, Charles C Thomas, Publisher, 1958

TRICHOMONIASIS

To the Editor —*Is there any correlation between vaginal trichomoniasis in women who have and who have not had the cervix uteri removed? It is my impression that trichomoniasis is rare, or never found, in a woman whose uterine cervix or fundus has been removed Should treatment be aimed primarily at the endocervix?*

Leonard J Janis, M D, San Diego, Calif

Answer —Trichomonas vaginalis infection of the vagina, frequently present subclinically, may become symptomatic when changes in acidity secondary to menstrual discharge, chronic cervicitis, chemical irritants, and trauma favor the growth of the organism Elimination of discharge from erosions of the portio vaginalis of the cervix and endocervix frequently cures the infection, but it may occur in the absence of a cervix uteri when other factors are present Treatment of the cervix alone may be satisfactory and curative in many instances, but in resistant cases the marital partner must also be treated

SAILING IN SUNNY WATERS

To the Editor —*A 16-year-old boy is going boat racing in southern waters in June He will be exposed at least 10 hours a day for several weeks to temperatures over 100 F Other than properly protecting his head from the sun, being well tanned, and replacing fluids and electrolytes lost through excessive sweating, what can he take or apply to the skin to prevent being overcome by the heat? He is from the northern part of the United States*

Gregori O Volovic, M D, Lowville, N Y

Answer —Proper head covering, being well tanned, and the ingestion of sufficient fluids and electrolytes to maintain a normal volume (about 1,500 ml) of urine during each day is all that the boy can do to prepare for the race A period of acclimatization (1 to 2 months) would be a good prophylactic measure I know of no substances that could be applied to the skin to prevent heat injury In fact, I would advise against the use of any kind of applications to the skin

Answer —In addition to heat exhaustion, the problem of sunburn must be considered It is well known that water scatters sunlight, thereby increasing the dosage of a given exposure Therefore, a person seemingly protected by a head covering or beach umbrella could be exposed to the burning rays of the sun Furthermore, while a tanned skin offers some protection, the degree of protection in any one person cannot be measured Ten hours in the sun daily for several weeks in June constitutes prolonged, intense exposure Both clothing and sun screening chemicals should be used to provide maximum protection

DEEP IRRADIATION

To the Editor —*If an area of the abdomen measuring 12 by 15 cm is treated, would the skin dose of irradiation be greater when the cone is placed directly on the skin or when the patient's clothes are interposed between the surface of cone and the skin?*

Walter L Cawood, M D , Ashland, Ky

Answer —The depth at which radiation dosage reaches its maximum depends on the energy of the radiation beam For conventional voltages used for deep therapy—200 to 250 kv , with added filter of 0 5 to 2 0 mm of copper (half-value layer of 1 0 to 3 0 mm of copper)—the maximum dose is within the first millimeter of skin or tissue equivalent material interposed at the skin surface This phenomenon is due to the build-up of electron equilibrium For x-ray therapy beams with energies of 2 million volts or equivalent, as telecobalt radiation, the maximum dosage point is several millimeters below the surface and produces the effect of skin sparing Therefore, in treatment with conventional deep therapy, a thin layer of clothing over the treatment area may be desirable With megavoltage therapy, however, the skin-sparing effect may be lost if an appreciable thickness of clothing or other material is present in the beam, close to the skin In both cases, however, the treatment portals can usually be placed more accurately if the skin is exposed

For more complete discussion of this problem and tables on the dosages at various depths, see standard textbooks of radiologic physics such as "Physical Foundations of Radiology" by Glasser and co-authors (New York, Paul B Hoeber, Inc , 1952) and "Radiation Dosimetry" by Hine and Brownell (New York, Academic Press, Inc , 1956)

DENICOTINIZED CIGARETTES

To the Editor —*A patient has asked about denicotinized cigarettes and their effect on peripheral arteriosclerosis This man has had a bilateral sympathectomy and wants to resume smoking, but his vascular surgeon advises against it*

William E Swift Jr , M D , New Haven, Conn

Answer —Any patient who has peripheral occlusive arterial disease severe enough to justify sympathectomy should not use tobacco in any form, irrespective of whether it is denicotinized The nicotine content of denicotinized cigarettes, though lower than in most standard brands, is still high enough to produce peripheral vasoconstriction when they are smoked This is detrimental to patients with occlusive arterial disease

REMOVAL OF ADHESIVE TAPE

To the Editor —*What ordinary household materials or solutions can be safely used to help remove adhesive plaster from the skin?*

M D , New Jersey

- Answer —Dry-cleaning fluids containing carbon tetrachloride would be undesirable because of possible skin absorption as would be ordinary gasoline, which contains tetraethyl lead White gasoline, on the other hand, does not contain lead Lighter fluid would be an efficient adhesive remover

GLYCOLYSIS

To the Editor —*At what rate does glycolysis occur after preparation of a filtrate for determination of blood glucose as compared to the rate of glycolysis for whole oxalated blood? Can a technician safely prepare filtrates in advance and run an entire group after permitting them to stand at room temperature for three or four hours?*

Norman G Schneeberg, M D , Philadelphia, Pa

Answer —The rate of glycolysis after preparation of a filtrate for determination of blood glucose is low, and for practical purposes insignificant Destruction of glucose in blood filtrates occurs only after growth of bacteria takes place This should not occur in three or four hours at room temperature, and therefore it is perfectly safe to allow the filtrates to stand for that period before running the glucose analysis

RACE AND ADOPTIONS

To the Editor —*I am in charge of the adoptions for one of the family service organizations There have been several instances in which there was a question whether the father of a child might have been Negroid Is there any definite method to ascertain whether a child may have a Negro ancestry? Also, is it possible for a person with some Negro blood to be the parent of a child of much darker skin color?*

Robert S Easton, M D , Peoria, Ill

Answer —There is no certain method of telling whether the father of a child has a Negro ancestry It is possible, although unusual, for the offspring of a person of dark skin color to be darker than the parent

RADIOACTIVE STRONTIUM

To THE EDITOR —*A report in the N Y Times, Sept 4, 1959, first page of the second section, states that Atomic Energy Commission scientists have found whole-wheat bread to contain roughly three to four times as much radioactive strontium 90 (Sr^{90}) as does white bread The figures for whole-wheat bread were as high as the highest found in milk samples or slightly higher The tests were made in May by the Health and Safety Laboratory of the commission's New York Operations Office In terms of possible human hazard the figures are generally considered low Would it be advisable to substitute white for whole-wheat bread in view of the higher amount of Sr^{90} in whole-wheat bread?*

Charles C Graves, M D , Broomall, Pa

ANSWER —The best estimates for a lifetime exposure of population groups to Sr^{90} as announced by the Public Health Service in July, 1959, noted that its maximum permissible limit for drinking water was 80 micro-microcuries per liter With an average water intake of 2 liters per day as food and liquid, the intake from this source might approximate 160 micro-microcuries per adult per day The values reported for whole-wheat bread ranged from 37 to 59 micro-microcuries per kilogram On this basis and assuming absorbable strontium to be the same in water and bread, some 5 to 10 lb of bread would have to be eaten daily to provide a like amount These comparisons suggest that an estimated reasonable margin of safety exists for whole-wheat bread

CEPHALALGIA

To THE EDITOR —*In your section of* THE JOURNAL, *March 26, page 1464, your excellent answer to Dr Bruce McIntyre, of Whitefish, Mont, should have included the possibility of functional hyperinsulinism as the cause of this patient s cephalalgia In the past four years I have treated about 600 patients with functional hyperinsulinism, and one of them had undergone neurectomies for relief A six-hour glucose tolerance test in this patient with headache of 18 years' duration revealed a blood sugar drop to 49 mg per 100 ml at the fourth hour*

Another patient with intractable right-sided headache of two years' duration had been given a misdiagnosis of temporal arteritis, and one neurosurgeon sectioned the right temporal artery A second neurosurgeon made a diagnosis of second cervical root syndrome and performed a laminectomy for removal of bone spurs impinging on nerve root foramens Neither operation helped because on the six-hour glucose tolerance test there was a blood sugar drop to 25 mg per 100 ml at the fourth hour Both of these patients recovered in a matter of a few weeks on a modified Seale Harris diet Patients with blood sugars at these levels will also have mood reactions characterized by tension, desperation, exhaustion, resentment, hostility, and anxiety

Harry M Salzer, M D
6056 Montgomery Road
Cincinnati 13

The above comment was referred to the consultant who answered the original question, and his reply follows —ED

To THE EDITOR —*I quote from page 204 of Wolff's "Headache and Other Head Pain" (Oxford University Press, 1950)*

"b In a small series of subjects, Kunkle and Barker of the New York Hospital demonstrated that there is a relation between headache, food deprivation, the blood-sugar level and threshold of jolt headache Food deprivation, either with or without a fall of blood-sugar level, may be associated with lowering of the threshold Thus, in one subject after eight hours of fasting the jolt headache threshold dropped from 7 0 to 5 1 g In another subject, after insulin injected intravenously, when the blood-sugar level fell from 85 to 24 mg /100 cc , the threshold of jolt headache fell from 5 9 to 3 3 g And inversely, after ingestion of 50 gm of glucose, when the blood-sugar level rose to normal (95 mg /100 cc) the threshold of jolt headache also rose to 6 3 g These data further support the view that hunger headaches stem from pain-sensitive intracranial vessels"

Moreover, there is other evidence to support the view that hunger headache, with or without lowered blood glucose, is of vascular origin

It is a common observation that the hunger from missing a meal is associated with fatigue, tension, irritability, and sometimes mood change, and it is in such a setting that headaches of the vascular type or of the muscle tension type may develop I would not consider functional hyperinsulinism per se as a common cause of headache

HYPERHIDROSIS IN AN ELDERLY PATIENT

To THE EDITOR —*The answer to the query regarding Hyperhidrosis in an Elderly Patient in* THE JOURNAL, *Feb 6, page 640, might have included the possibility of pheochromocytoma Although the information supplied in the query is meager, the borderline diabetic condition plus the profuse sweating episodes are suggestive enough to warrant at least several determinations of urinary catecholamine levels*

In the past year, a patient who had profuse sweating as her chief complaint for 12 years, has been given complete and exhaustive studies at *two university hospitals, including screening and provocative tests for pheochromocytoma, except for omission of assay of urinary catecholamine levels Her blood pressure varied between normal and mild hypertensive levels She had no truly paroxysmal attacks The primary sign and symptom was perspiration, which persisted day and night Examination of the urine for pressor amines revealed high levels At exploratory operation a pheochromocytoma of the right adrenal gland was found and removed After the operation, the patient's skin was dry for the first time in years*

Milton A Bell, M D
5136 Wayne Avenue
Philadelphia 44

SIDE-EFFECTS OF GRISEOFULVIN

To the Editor —*Our experience with the use of griseofulvin indicates that there may be undesirable side-effects During long-term treatment as for fungus infections of the nails, lapse of attention and of recent memory have occurred A patient who had been taking the drug for two months found himself forgetting routine but important details in flying a jet aircraft His wife noticed that his coordination was poor and that his driving ability had deteriorated The pilot himself felt that his daily activities, usually reflex in nature, required concentrated thought for proper performance He was grounded during the course of treatment*

This should be brought to the attention of all physicians using griseofulvin lest we find ourselves contributing to our nation's toll of accidents

Richard M Fenno, M D
Headquarters Twelfth Air Force
United States Air Force
Waco, Texas

The above comment was referred to the consultant who answered the original question, and his reply follows —Ed

To the Editor —*It would be interesting to know whether this is an isolated incident or whether such unusual side-effects are to be expected in any significant numbers I am inclined to think that side-effects of this type will be few in view of the fact that there have been no reports from other sources regarding this particular type of psychic aberration The letter does, however, sound a note of caution, and should put physicians on the alert for the possibility of such reactions*

IMMUNIZATIONS BEFORE GOING TO EUROPE

To the Editor —*In answer to the question "Immunizations Before Going to Europe," in the Questions and Answers section in* The Journal, *May 7, page 126, it is stated that immunization against typhoid should not be necessary for a person who has had the disease The literature is replete with instances of second attacks of typhoid, of typhoid after vaccination, and even of typhoid twice after vaccination (Marmion and others, J Hyg 51 2 [June] 1953) Protection is a function of the current immune status of the subject and the amount of exposure to the agent Immunity is relative and can be overcome by large enough doses of typhoid organisms*

Major Jerome H Greenberg, M D
Department of the Army
Office of the Surgeon General
Washington 25, D C

ENTERITIS IN TOURISTS

To the Editor —*In the Question and Answer on "Enteritis in Tourists,"* The Journal, *May 7, page 128, the question refers to mild enteritis in American tourists in Mexico One answer states "Ordinarily the cause is associated with staphylococcic or streptococcic contamination of food, with resulting production of clinical toxins which are highly irritating to the intestinal mucosa" Staphylococcic contamination of food usually produces, not mild enteritis, but a rather severe bout of nausea and vomiting with or without diarrhea The severity depends on the amount of toxin ingested and individual sensitivity Streptococcic infections transmitted in food most commonly produce typical streptococcic sore throat, not mild (or severe, for that matter) enteritis The mechanism in this case is direct infection by the streptococcus, with the toxin, if any, playing only a secondary role, as in scarlet fever The etiological factors in diarrhea of tourists probably include mechanical irritation of the intestine by spicy foods and oils to which the traveler is not accustomed, and infection with one or more of various agents such as Shigella, Salmonella, and assorted viruses*

Major Jerome H Greenberg, M D
Department of the Army
Office of the Surgeon General
Washington 25, D C

CHEWING GUM IN EYELASHES

To the Editor —*With regard to the problem posed by Dr Sparks in* The Journal, *April 16, page 1874, my doctor suggested the application of any bland, pure cooking oil when my 2-year-old son had chewing gum in his eyelashes This proved to be simple and effective*

Mrs Milton Nelson
129 Clove Rd
New Rochelle, N Y

Editor's Note Many other readers have written to say that, if the gum is chilled with an ice cube, it becomes brittle and can be removed with ease

ABSTRACTS FROM THE LITERATURE

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Deficiency Amblyopia in the Alcoholic Patient —Observations have been made on a group of 14 alcoholic patients, all of whom had an ocular disorder characterized by an impairment of central vision and the presence of central and centrocecal scotomata which were more prominent with red and green than with white test objects Considerable recovery was the rule despite continued drinking and smoking The essential pathological change as observed in 1 patient was a degeneration of both optic nerves, chiasm and tracts limited to the pathway of the papillomacular bundles It is evident, from our data and that of others, that nutritional deficiency, rather than the toxic effects of alcohol, tobacco or both, is the cause of this ocular disorder and that deficiency and tobacco-alcohol amblyopia are clinically and pathologically identical The specific nutrient or nutrients responsible remains to be discovered

Lacrimal Gland Response to Parasympathomimetics —This problem was studied in experiments on 4 patients with facial paralysis As the site of the interruption of the 7th nerve was situated far above the geniculate ganglion the parasympathetic nervous supply of the lacrimal gland could be considered to be discontinued Parasympathomimetic agents were administered subcutaneously and lacrimal secretion was determined by means of Schirmer s test The reaction of the denervated glands to pilocarpine and mecholyl was such as to allow the conclusion to be drawn that the glands were sensitized to direct parasympathomimetics but the denervated glands did not to any appreciable degree react to neostigmine in a dosage which elicited responses from the contralateral normal glands Instillation of cocaine into the conjunctival sac was followed by a decrease of lacrimal secretion which had previously risen under the influence of pilocarpine

Vascular Lesions of the Visual Cortex —Posterior cerebral artery compression may result from herniation of the brain through the tentorial incisura, caused by increased pressure above the tentorium Such compression produces visual cortical infarction and expresses itself clinically as homonymous hemianopsia Seven patients with such hemianopsia were reported, each had increased pressure from lesions above the tentorium, and dulling of consciousness or coma during the onset of the visual field defect All visual defects had a visual cortical character In no patient could the field defect be satisfactorily explained by direct involvement of the postchiasmal visual pathways by the tumor, brain trauma or subdural hematoma Visual cortical hemianopsia occurring during or after an episode of high pressure above the tentorium may indicate present or past compression of the posterior cerebral artery Such field defects may confuse rather than clarify the localization of a supratentorial mass

Perilimbal Ulceration in Wegener s Granulomatosis —Both eyes of a patient with Wegener s granulomatosis were observed clinically and found to have progressive perilimbal ulceration of the sclera, cornea, and iridocyclitis Histopathological study of these eyes revealed necrosis of the sclera and marginal cornea, apparently resulting from occlusion of the anterior ciliary vessels by a necrotizing angiitis indistinguishable from periarteritis nodosa In addition granulomata characterized by necrosis, epithelioid cells, and multinucleated foreign-body-type giant cells were found within the ciliary body, adjacent to the ulcerated sclera The findings suggest that these granulomata may have formed in response to the necrotic scleral tissue as a form of auto immune reaction The presence of marginal corneal and scleral ulcers, especially in the presence of pulmonary disease, should suggest the possibility of Wegener s granulomatosis or of one of the related necrotizing angiitides

Pigmentary Retinopathy After A New Phenothiazine —Of 29 psychiatric patients treated with a new phenothiazine (thioridazine) 4 of 5 patients on a total dose in excess of 85 gm developed ophthalmological complications Subjective complaints of diminution of light intensity and loss of vision, severe in 2 patients, were elicited in all 4 Extensive pigmentary retinopathy developed in all Special studies in the 2 more seriously affected individuals revealed that the visual receptors were severely involved Administration of different vitamins and steroids did not alter the course of this retinopathy High concentration of phenothiazine in the uvea and a specific enzyme inhibition possibly associated with the piperidine ring in the side chain of the phenothiazine, may be the responsible mechanism

Macroglobulinemia with Unusual Vascular Changes —The characteristic retinopathy of macroglobulinemia consists of venous dilatation and tortuosity, hemorrhages and occasional central or branch vein occlusions A patient with macroglobulinemia exhibited the characteristic retinopathy plus unusual aneurysmal dilatations of the retinal arteries and microaneurysms of the peripheral veins The diagnosis was confirmed by ultracentrifuge analysis and electrophoresis The patient had been seen 9 months previously at a large midwestern clinic, and a diagnosis of dysproteinemia had been made At that time he had the characteristic retinopathy of macroglobulinemia but did not have the aneurysmal dilatations of the retinal arteries or the microaneurysms Since there were no other findings to explain the retinopathy and since the retinopathy developed during the course of the disease, the retinal changes were considered to be an unusual manifestation of macroglobulinemia

Comparative Anatomy of the Ciliary Nerves—Recent studies in the field of ocular physiology have shown that a detailed knowledge of the anatomy of the ciliary nerves in different species of experimental animals is required for effective pursuit of experimental procedures Therefore the distribution of these nerves has been investigated by dissection of the orbital contents of a large number of rabbits, cats, and monkeys A smaller number of preparations from human sources was also examined Dissection of the orbital content was facilitated by selectively staining the nerves, using a modification of Christensen's silver method Comparison of the ciliary nerves in the experimental species showed a common pattern, but variations from species to species were striking The greatest differences were in the size and accessibility of the ciliary ganglion and in the degree of fusion of the sympathetic and sensory nerves with the ganglion or postganglionic branches

Changes in Crystalline Lens Caused by Autolysis—Autolytic changes were observed in histological preparations of the crystalline lenses of rats that had been dead for various periods of time These changes were noted within one-half hour after death and became proggressively more severe during a 12-hour period The first autolytic changes were noted in relation to the nuclei at the equator Later abnormalities were found to involve the fibers throughout the cortex but seemed to be more severe in the posterior part of the lens High blood sugar levels at the time of death appeared to intensify the autolytic changes The pH of homogenized lens tissue was lowered within 3 hours after death This lowered pH may be associated with the autolytic changes

Effect of Alpha-Chymotrypsin on Corneal Wound Healing—Alpha-chymotrypsin has been shown to facilitate intracapsular cataract extraction by a proteolytic action on the zonular fibers of the crystalline lens Reports have appeared indicating delayed wound healing following use of the enzyme This experimental study was undertaken to determine the effect of alpha-chymotrypsin on experimentally induced corneal wounds Cats were used as the experimental animals Corneal incisions of a specific length were made and tied with a preplaced corneal suture Three days after surgery, the wounds were disrupted, and the force to accomplish this disruption was quantitatively measured No statistical difference (*t* test) was found between 18 control and 18 experimental animals It was noted that a fibrin clot formed in the anterior chamber after irrigation with enzyme This complication was avoided by prophylactic flushing of the anterior chamber with normal saline prior to irrigation with the enzyme This practice could be clinically applied

Electrophoresis of Subretinal Fluid—Subretinal fluid in the presence of a retinal hole has been classically considered to be vitreous fluid which has percolated through the hole This is a report of 20 cases of retinal detachment in which the subretinal fluid was studied by paper electrophoresis Retinal holes were visualized in 17 of these cases Normal vitreous and aqueous contain so little protein that one can scarcely detect a pattern with this technique Subretinal fluid, on the other hand, shows a pattern not unlike that of normal serum Simple percolation from the vitreous does not appear to explain the mechanism whereby subretinal fluid protein concentration becomes so markedly elevated above the levels found in normal vitreous

Nerves of the Normal Human Choroid—Histological studies of the normal human choroid with the nerve fiber stain of del Rio Hortega revealed two general types of nerve fibers (1) fibers which branch off the ciliary nerves in small bundles and run in the intervascular spaces of the choroid and (2) perivascular nerve fibers These two types of nerves were found to be interconnected However, they seemed to represent two somewhat different nervous systems of the choroid Branches of the first nerve type were seen to form very delicate terminal networks on the outer surface of Bruch's membrane No conclusions as to the nature and function of the two different types of choroidal nerves could be drawn from the histological observations

Intraocular Pressure and Outflow Facility—In 32 freshly enucleated eyes of the rabbit and cat the facility of outflow was found to decrease exponentially as the intraocular pressure linearly increased The effect on facility was immediate and reversible, it was independent of the washing effect of continuous perfusion or of precipitation in the filter Hyaluronidase increased outflow facility but did not reduce the effect of pressure on facility of outflow In 6 eyes the effect was absent when the pressure was raised by injecting fluid into the anterior chamber directly but appeared when it was introduced from behind the iris diaphragm The recovery from the effect of increased pressure on outflow facility was not always complete but could be made so by quick temporary reduction in pressure

Latex Agglutination Test in Uveitis—Beta hemolytic Streptococci have been incriminated in rheumatoid arthritis and non-granulomatous uveitis Rheumatoid arthritis has been found in as high as 20% of cases of uveitis The latex fixation test for rheumatoid arthritis, accordingly, recommended itself for evaluation in clinical uveitis The test was performed in 151 consecutive cases of endogenous uveitis Positive tests in titers ranging from 1 20 to 1 640 were found in 31 cases Eleven of the 58 non-granulomatous and 20 of the 93 granulomatous cases had positive tests Rheumatoid arthritis was found in 16 cases, 6 in the non-granulomatous and 10 in the granulomatous categories Positive tests were found in 10 of the 16 cases of arthritis Obviously no type of uveitis was favored with positive results, and the test has little to offer as a routine procedure in uveitis

The Embryogenesis of Ectopic Lentis—Marfan's syndrome of congenital cardiovascular anomalies, skeletal aberrations, and ectopia lentis has been thought to be a result of mesodermal defects This concept was established in studies of the cardiovascular manifestations in which an abiotrophy of elastic tissue was found This case is presented to corroborate this postulation The usual signs of Marfan's syndrome were present plus the findings of skin lesions, which biopsy revealed to be elastic tissue degeneration This skin manifestation appears to substantiate the previous theory of the embryonic defects responsible for the signs of Marfan's syndrome

Hematologic Toxicity of Daraprim (Pyrimethamine)—The hematological effects of pyrimethamine therapy were observed in 87 cases treated with pyrimethamine and sulfonamides for possible Toxoplasma uveitis Although some degree of anemia, leukopenia, and thrombocytopenia were frequently observed, the drop in platelet count was the most important clinical manifestation of pyrimethamine toxicity The incidence of hematological changes was related to dosage but disappeared spontaneously after the cessation of therapy

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Nasal Physiology and Corrective Nasal Surgery—Standardized objective tests are needed for the useful evaluation of nasal function Clinical history, reports and examinations, by themselves, are not valid for statistical studies In addition to the well known functions of the nose, there are at least 15 others to be added that need easy methods of testing At the present time we are exploring 3 (1) nasal pressures as registered at the nostrils, (2) changes of these pressures brought about by changing the position of the head, (3) pressures developed as the air flowing through each nasal chamber (on inhalation and on exhalation) ranges from 2 to 8 liters per minute Studies so far have been very helpful in furthering understanding of the normal role of the nose in respiration and homeostasis

Bilateral Hearing Aids for Monaural Total Deafness—The author describes a simple way to enable people who have a total deafness or no useable hearing in one ear but some useable hearing in the other ear, to locate the direction from which sounds are coming in spite of the fact that they do not have binaural hearing This is accomplished by bringing to the hearing ear sounds from the opposite side of the head It may be done in several ways, and very nicely, by mounting a microphone on both templets of an eyeglass hearing aid, and connecting both to the receiver which is in the serviceably hearing ear The position of the microphones is important A bilateral but not a stereophonic effect is produced However, the patient will be able to hear (or hear better) sounds coming from any direction and with practice locate the source of the sounds There are several other advantages in this bilateral arrangement and these are described

Humidification Indoors in Winter—The purpose of this study is to present ways and means of humidifying our living quarters In winter, when the cold outside air has been brought indoors and heated, its relative humidity is greatly reduced This extreme dryness causes many ills, particularly upper respiratory ills Achieving proper humidity has often been very difficult The so called humidifiers that come with most (hot air) furnaces give out so little water that they are usually worthless A gallon or more a day per room has been found to be required The various methods available for humidification, the problems likely to be met and their solution have been discussed

Surgical Treatment of Otosclerosis—This report involved a statistical analysis of the clinical and audiometric results of 5 years experience with otologic surgical procedures designed to alleviate otosclerotic deafness The preoperative and postoperative hearing test results of 688 surgical cases were arranged and analyzed according to type of procedure done and audiological results of the surgical procedures studied were (1) Rosen tilt technique, (2) pressure procedures, (3) microscopy and the use of chisels, (4) footplate trephination of Rosen, (5) bypass procedure of Shea and (6) fenestra ovalis vein graft technique of Shea The results of this study indicated that each successive development in stapes surgery produced a better incidence of successful restoration of hearing acuity In addition it showed that conservative procedures cannot successfully cope with diffuse otosclerosis The study further demonstrated that the bypass or anterior crurotomy technique produces better hearing in cases of localized otosclerosis than do earlier techniques, and that the Shea fenestra ovalis procedure is best suited to manage diffuse otosclerosis

Chronic Frontal Sinusitis—The differential diagnosis of obliterative frontal sinus disease includes chronic proliferative osteitis and fibrous dysplasia, among others Osteogenesis associated with chronic infection may go through a preliminary stage of osteoid with a later deposition of calcium reportedly capable of going on to complete ossification with healing of the primary infection This appears to be one way nature attempts to handle chronic infection in the frontal and ethmoid sinuses The x-ray picture in late stages may be misinterpreted as agenesis Two cases were presented of an intermediate stage in which osteoid occupied the sinus lumen with the mucosal lining reduced to narrow fingers A bony fistula complicated in both cases Fibrous dysplasia was ruled out by history and by gross and microscopic pathology Obliterative surgery (Riedel) was performed Gelfoam packing to restore contour was tried with partial success

Two Antihistamines in Allergic Rhinitis—The published reports on new antihistamines often leave much to be desired They often fail to give a comparison with any known effective preparation To remedy this, a method for evaluating antihistamines on the double blind comparison method was developed It was helpful in eliminating some of the variable factors usually encountered Parabromdylamine maleate in 8 mg size (Dimetane) was compared to tripelennamine 50 mg (Pyribenzamine) Both antihistamines proved satisfactory therapeutic agents Parabromdylamine maleate had the lower incidence of side-effects and a higher degree of patient acceptance

Cancer of Larynx, Pharynx, and Esophagus—The method of treatment for cancer of the larynx, pharynx and esophagus is dependent upon a comparison of known end results currently available Early cancer of the true cord is better treated by irradiation since functional results are good and the cure rate is as high or higher than that by surgery Elective and therapeutic neck dissections have been carried out in all instances of advanced laryngeal cancer These end results were compared with laryngectomy alone and there was an improvement in 5-year survivals in the elective neck dissection series the survival rate for the endolarynx was 69%, compared to laryngectomy alone with results of 50% This means that a 19% increase of survival is possible with elective neck dissection Likewise there was a 5-year cure rate of 59% for subglottic cancer compared to 42% for laryngectomy alone

Myxedematous Hoarseness—Myxedematous hoarseness is characterized by a lowering of the pitch and a diminution in the clearness of the voice It has been observed that the voice changes may be very gradual and insidious in onset in the aged person The changes will occur only when there is a subnormal lowering of the thyroxin level of the blood As long as the thyroxin in the circulating blood is adequate for maintenance of a harmonious physiological balance, myxedematous hoarseness will not occur However, when the period of thyroxin deficiency manifests itself and there is either external or hidden evidence of incipient myxedema, then hoarseness may manifest itself It is emphasized that myxedematous hoarseness occurs about 10 days before the clinical picture of myxedema is in evidence In our patients, 'puffiness' under the eyes is the 1st sign of clinical myxedema The 2nd sign is coarseness of the skin with flabby underlying muscles The clinician should not wait until all the edematous changes become visible Therapy should be administered as soon as the diagnosis of myxedematous hoarseness is made Treatment consists in the administration of adequate doses of thyroid extract It may be necessary to give 3 or 4 grains daily to an adult with myxedema The dosage of thyroid extract can be lessened as the patient improves and then a maintenance dose can be prescribed

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Evaluation of Nitrites in Treatment of Angina Pectoris H I Russek	p 478

Nitrites in Treatment of Angina Pectoris—The 58 patients selected for this study presented classical symptoms of angina pectoris which responded to the prophylactic and therapeutic administration of nitroglycerin Each patient was treated with a separate course of erythrityl (erythrol) tetranitrate (ETN) (15 mg) and a placebo The tablets were administered sublingually or in the buccal pouch 3 times daily, after meals, in courses of 2 weeks each The first course was invariably a placebo A drawback in the use of ETN sublingually was that 40% of the patients were troubled with headache, which necessitated the interruption of ETN therapy in almost half of the patients, but in the remainder headache disappeared as tolerance developed or when dosage was reduced from 15 to 7 5 mg Treatment should, therefore, be initiated with this lower dosage The magnitude of the response to pentaerythrityl (pentaerythritol) tetranitrate (PETN) in 8 patients was similar to that observed with ETN sublingually, but the time of onset and duration of action of the drugs differed PETN required an hour or more after oral ingestion to produce effect, but its action persisted twice as long as that of ETN When given sublingually, PETN had an immediate but relatively brief vasodilator effect PETN given orally was superior to ETN sublingually in its relative freedom from side-effects and in its more prolonged action Its chief disadvantage is the lag in activity ETN because of its rapid effect is, like nitroglycerin, suited for prophylactic administration prior to exertion For this purpose one 15 mg tablet of ETN sublingually has the effect of 4 to 6 nitroglycerin tablets administered singly at 20-minute to 30-minute intervals Suggestions are made for correcting inadequacies in PETN administration and for combining ETN and PETN to give continuous prophylaxis

American Journal of Pathology, Ann Arbor, Mich.

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Changes in Hepatic Structure in Wilson's Disease—Histological observations of the liver of 20 patients with hepatolenticular degeneration (Wilson's disease) indicated that the cirrhosis associated with this condition is postnecrotic in type, with stages varying from those which are completely arrested to others which are very active A tabulated report of the histologic features in the various stages of cirrhosis in Wilson's disease shows that the process was arrested in 5 patients, partially arrested in 6, active in 7, precirrhotic in 1, and acute parenchymal breakdown existed in 1 For comparison, 15 examples of active postnecrotic cirrhosis not associated with Wilson's disease were gathered from the necropsy files of the Mount Sinai Hospital, New York In all necropsy specimens from cases of hepatolenticular degeneration, the typical lesion of postnecrotic cirrhosis was found This was characterized by 3 cardinal manifestations (1) irregular distribution of the postnecrotic alterations as reflected by preserved lobular architecture in many nodules, (2) stromal collapse with the formation of septums of varying width, (3) conspicuous parenchymal regeneration Features not found in other types of postnecrotic cirrhosis are degeneration of fat-containing liver cells, the appearance of excessively large Kupffer cells, and glycogen degeneration of the liver cell nuclei The fatty metamorphosis and nuclear alterations apparently precede the development of cirrhosis and appear to contribute, at least in part, to the necrosis and stromal collapse characteristic of postnecrotic cirrhosis in Wilson s disease

Annals of Internal Medicine, Lancaster, Pa

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Course of Mitral Stenosis Without Surgery —The authors report on 250 patients who were treated medically in the presurgical era, and who were followed until death or for a minimal period of 10 years 115 patients were followed for 20 years The patients were divided into 4 groups in accordance with the grades of severity existing at the first examination (1) auscultatory signs of mitral stenosis without symptoms and with normal rhythm 52%, (2) mild symptoms with normal rhythm or atrial fibrillation, 37% (3) moderate to moderately severe symptoms or a major complication, 10%, (4) chronic heart failure, 1% Eighty-three patients were under 20 years of age The predominance of young and asymptomatic patients is due to the inclusion of 108 cases from a unit of Children s Medical Center Except for the asymptomatic patients (grade 1), each group had its highest mortality in the first 5 years Of the entire series, 61% lived 10 years of those with grade 1 lesions, 84% lived 10 years, grade 2, 42% and grade 3, 15% After 10 years, two-fifths remained in the same grade of severity as before, two-fifths had died, and one fifth had progressed to a category of greater severity At the end of 20 years 80% had died and the status in 13% was unchanged Sixty-seven patients died of progressive heart failure 21 died of arterial embolism and 10 of single or multiple pulmonary embolism Five patients succumbed to subacute bacterial endocarditis before the antibiotic era The remainder died of unrelated disease In comparing the survival records 7 years after surgical treatment with those of the medically treated patients, the sustained benefits of mitral valvulotomy are evident

Obesity and Diabetes —Obesity is the most important of the precipitating and aggravating factors in the form of diabetes that is relatively mild and occurs in patients of mature age This form is frequently treated with orally administered hypoglycemic agents, but the author feels that more stress should be placed on the importance of weight reduction than on a substitute for insulin Recent reports on the safety of the anorexigenic agent, phenmetrazine hydrochloride induced him to carry out a controlled investigation on this agent A triple-blind study was begun on 80 obese diabetic patients The 3rd blind factor added to the usual double-blind procedure was unawareness by the patients of any relationship between the medication and appetite or caloric intake The medication was discontinued in 5 patients after from 1 to 6 weeks because of side-effects An additional 21 patients were not suitable for final analysis because of poor cooperation or because they had edema, which made weight studies impossible The remaining 54 patients in the 2 groups, 29 on phenmetrazine and 25 on placebo medication, were comparable as to age and type of diabetic control Twenty-three of the 29 lost a significant amount of weight, as opposed to 3 of 25 in the placebo group Fifty per cent of the insulin-taking patients in the phenmetrazine group had their insulin dosage reduced 50 to 100%, as opposed to none of the placebo group The value of a pharmacologically active anorexigenic agent such as phenmetrazine hydrochloride in the management of obese diabetic patients would seem to be preferable to that of oral hypoglycemic agents

Corticotropin in Myasthenia Gravis —The author reports on 6 patients with myasthenia gravis treated with corticotropin Fifty units of corticotropin gel were injected twice daily for 5 days but if there was any difficulty in breathing or swallowing, the aqueous form was injected so that the effect of the hormone could be halted quickly if the symptoms became alarming Neostigmine was usually administered in the same dosage as before but frequently this dose had to be lowered A low sodium diet was prescribed, and 2 or 3 Gm of potassium chloride was given daily These measures seemed to decrease the extreme weakness which often developed during treatment Five of the 6 patients showed improvement Four of those who were helped initially have been treated many times since, with benefit every time The duration and degree of benefit varied The sequence of events in those who received benefit was that for the 1st few days there was a feeling of slightly increased strength During the last 3 days and for a day after the last dose the myasthenic symptoms became progressively worse, so that occasionally treatment had to be stopped before the course was completed About 3 days after the last dose of corticotropin, diuresis appeared accompanied by increasing strength, which became maximal on the 7th day In the next few weeks this increased muscular power waned somewhat, but did not return to its former low level for a period of several months, and often for as long as a year The author recommends reevaluation of corticotropin therapy in selected patients with myasthenia gravis, chiefly in those without prominent bulbar weakness Not only the thymus but also other lymphatic tissues might be the source of the myoneural toxin of myasthenia gravis Corticotropin may act by causing lysis of these tissues

Brucellosis —This study concerns 224 patients with brucellosis who were examined at the Mayo Clinic between 1940 and 1958 Brucella organisms were isolated from the blood of 47 patients, and from specimens taken for biopsy or from aspirations in 42 patients Eighty-one patients had an antibrucellar agglutination titer of 1 1,280 or more but Brucella organisms could not be obtained from them by culture Fifty-four patients yielded antibrucellar agglutination titers ranging from 1 200 to 1 800 In the central portion of the United States brucellosis is mostly an occupational disease That contact with infected animals, especially the products of conception of such animals, rather than ingestion of contaminated milk products was responsible for the majority of brucellar infections was suggested by the fact that most of the patients were engaged in occupations related to animal husbandry Most of the infections were caused by B abortus or B suis, and only a few were caused by B melitensis Most of the patients with bacteremic brucellosis exhibited the clinical manifestations of severe systemic infection In patients with localized brucellosis the agglutination titers often were low or absent B Suis was the strain of Brucella most commonly isolated from the localized lesions Results of treatment with a combination of tetracycline and streptomycin were satisfactory in patients who had bacteremic brucellosis Surgical drainage or excision of localized infections was of value in diagnosis and treatment

Systemic Lupus Erythematosus and Hypertension —The authors present the histories of 2 young patients with systemic lupus erythematosus (S L E) who had severe arterial hypertension without marked impairment of renal function Both failed to respond to antihypertensive therapy, which in 1 patient included subtotal adrenalectomy and subdiaphragmatic sympathectomy The clinical course of these patients suggested a collagen disease At autopsy, lesions compatible with lupus erythematosus were found in the heart and kidneys The physician should consider the possibility of disseminated lupus in patients with essential hypertension In reviewing the literature the authors found that occasionally, hypertension may occur in S L E even before skin manifestations, hepatosplenomegaly or pancytopenia appear It was not possible to ascertain whether, in their 2 patients, hypertension developed as a result of nephritis due to lupus which had not yet reached a stage of renal functional impairment, or whether they had essential hypertension The 1st of the 2 patients had renal lesions which the pathologist thought were typical of those seen in S L E In the 2nd patient, however, the over-all histologic appearance was more that of advanced chronic arteriolar nephrosclerosis The appearance of S L E late in the course may have been responsible for the terminal uremia A less attractive hypothesis is that progressive renal impairment from another cause might have occasioned an exacerbation of latent lupus

Arch orthop u Unfall-Chir, Munich

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Dislocation of Elbow and Its Late Sequels
H Benzer p 592
Osteochondromas and Exostoses After Irradiation
J Kolař p 631

Osteochondromas and Exostoses After Irradiation —The author made studies on 115 children who had received irradiations In 4 he found a typical exostosis or an exostosis-like lesion in bones that had been exposed to irradiation In the 1st child a hemangioma of the left thigh had been treated with a total of 4,165 r, when the child was 4 months old Eight years later, the femur was 15 mm shorter and structural irregularities were evident in the still open epiphyseal synchondrosis and in the metaphysis An exostosis the size of a pea was found 1 cm above the epiphyseal synchondrosis The 2nd child had received 1,768 r to each of 4 fields to counteract an extensive nevus flammeus above the left knee Seven years later the femur on the irradiated side was found to be 14 mm shorter, and there was an exostosis in the region of the metaphysis The 3rd child had received 2,360 r to each of 2 paravertebral fields after nephrectomy for nephroblastoma This boy 9 years later was found to have a sinistroconvex scoliosis of the lumbar spine, structural changes in the vertebrae, hypoplasia of the right side of the pelvis, and the right leg was 25 mm shorter There was also an exostosis in the form of an osteochondroma in the region of the tuberculum iliacum The 4th patient, at the age of 18 months, had received in the region of the right knee 3,480 r to each of 2 fields, for eosinophilic bone granuloma When the boy was 12 years old, examination revealed bone hypoplasia An 18 mm shortening of the fibula, structural changes in the region of the metaphysis, and an exostosis at the head of the fibula were found Surgical treatment is not necessary as long as the exostoses cause no complaints and show no abnormal growth, but they must be controlled at regular intervals, so that malignant growth tendencies may be detected early and the opportune time for surgical treatment will not be missed

British Medical Journal, London

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P S Gardner p 1077
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Nasal Staphylococci and Sepsis in Newborn Babies
P A Manfield and others p 1098
Aspirin as Cause of Anemia in Rheumatoid Arthritis
F D Baragar and J J Duthie p 1106

Viruses, Bacteria and Respiratory Disease in Children —The authors performed clinical, virologic and bacteriological studies on 146 children, between 6 months and 5 years of age, with acute respiratory diseases, who were admitted to hospital between January and June, 1959 Of these, 28 had upper respiratory infections (coryza, pharyngitis, tonsillitis, otitis media), 6 had croup, 37 had bronchitis, 27 had bronchiolitis, and 48 had pneumonia Except for the patients with acute bronchiolitis, evidence of infection by several different viruses was found in each of the other 4 groups, but no particular virus predominated No single virus was associated with any particular clinical finding such as meningism, muscle-ache, type of fever, or abnormal white blood-cell count The complete lack of evidence of virus infection in any of the 27 children with acute bronchiolitis may have been due to the authors' inability to test secretions from the lower respiratory tract, or to the presence of an unidentified virus Four of the 6 deaths which occurred among the 146 patients were due to acute bronchiolitis The croup-associated virus of Chanock and Beale was isolated from 4 children with clinical illness varying from mild upper respiratory infection to moderately severe pneumonia For the first time in Britain this virus was incriminated in the respiratory infections of children Potential bacterial pathogenic agents such as coagulase positive staphylococci, Hemophilus influenzae, pneumococci, and streptococci were isolated from the children in the 5 clinical groups, but their incidence was of the same order as in normal children

Trial of Adenovirus Vaccine in R A F Recruits —The authors administered commercially prepared trivalent adenovirus vaccine containing strains of types 3, 4, and 7 to 402 Royal Air Force recruits at Bridgnorth, England, in order to test its value Two of 5 flights of recruits arriving at Bridgnorth each week for 3 weeks during February, 1959, were inoculated Influenza A, influenza B, and adenovirus infections were all highly prevalent at Bridgnorth at the time the injections were given and during the weeks that followed The adenovirus strains isolated were predominantly type 3 There was a total reduction of 40% in the rate of admissions to the Station Sick Quarters for acute respiratory illness occurring in the inoculated flights of recruits more than one week after inoculation The protective effect of the vaccine against adenovirus infection, estimated from the results of isolation of virus, was 70% The value of adenovirus vaccine, previously shown among military recruits in the United States, has thus been confirmed in the Royal Air Force recruits

Aspirin as Cause of Anemia and Peptic Ulcer—The authors studied the variations in hemoglobin levels in 244 patients with rheumatoid arthritis admitted to hospital between 1948 and 1951 Most of these patients had been taking aspirin continuously or intermittently in varying doses for a number of years The patients were followed for 6 years with particular reference to their intake of salicylates and the incidence of dyspepsia and ulcer The patients showed a significant increase in hemoglobin level over the 6 year period Thirty-one patients who were known to have taken only very occasional doses of salicylates showed a similar increase in mean hemoglobin level to that shown by the patients who took adequate amounts of salicylates throughout the entire follow-up period At the final assessment, the hemoglobin level was below 80% in 27 patients In only 3 patients was there clinical or roentgenologic evidence of peptic ulcer Seven other patients had or were suspected of having an ulcer before rheumatoid arthritis developed The incidence of peptic ulcer in this series compares favorably with that in the general population It is concluded that most of the patients with rheumatoid arthritis can tolerate aspirin, when administered regularly, without an increase in anemia The dangers of causing peptic ulcer or of precipitating gastrointestinal hemorrhage appear to have been exaggerated

Circulation, New York

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Open Operation in Calcific Aortic Stenosis—After treating calcareous aortic stenosis by closed techniques and by an open technique with hypothermia, the authors have adopted an open technique utilizing extracorporeal circulation Their experience with the direct approach to the stenotic aortic valve began in January 1959 This report is based on 14 consecutive patients operated on at the Mayo Clinic between January and October 1959 One patient died during the operation and another died after leaving the hospital Of 7 patients followed for from 6 to 9 months after operation 6 showed symptomatic improvement A small improvement in the size of the valvular orifice can bring important benefits The open operation is advantageous because it avoids the creation of, or aggravation of, insufficiency while relieving stenosis The authors recommend this operation for patients whose disability is significant or progressing Severe coexisting coronary artery disease is a contraindication but associated aortic valvular insufficiency, advanced degrees of disability, and left ventricular failure are not

Direct Operation on the Aortic Valve—Muller and associates review the history of patients with aortic insufficiency and the clinical operations devised for its relief They feel that the multiplicity of morphologic forms demands individualization of the operative procedure for the specific type encountered Cardiopulmonary bypass is a prerequisite The authors describe and show illustrations of the methods used at the University of Virginia Hospital, Charlottesville, Va for treatment of aortic insufficiency These procedures include the release of the fixed valve leaflet and removal of calcium from it aortic valve leaflet extension with suture of a small piece of compressed polyvinyl sponge or Teflon fabric to the edge of 1 of the leaflets, excision and replacement of a portion of the valve with a synthetic leaflet, and complete subcoronary replacement of the valve with a prosthesis To relieve isolated rheumatic aortic insufficiency, an annulus has been constricted or a bicuspid aortic valve has been created Insufficiency resulting from perforation of 1 or more valve leaflets by subacute bacterial endocarditis has been treated by closure of the perforations Nineteen patients underwent 21 operations for the correction of aortic insufficiency All had suffered from, or were then suffering from, heart failure Several had significant coronary artery disease or multivalvular disease Eleven of the 19 patients are now well or greatly improved Eight died during or after the operative procedure A direct attack upon the insufficient aortic valve is the procedure of choice at the present time

Journal of Urology, Baltimore

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Carcinoma of the Bladder Modes of Local Invasion
H J Jewett and S L Eversole Jr p 383
Endocrine Therapy in Carcinoma of Prostate
J L Emmett L F Greene and A Papantoniou p 471

Heminephro-Ureterectomy—One hundred patients (their ages ranging from 4 months to 66 years) underwent heminephrectomy The entire ureter draining the affected segment was removed in 10 patients, while in the other 90 only the portion readily accessible through the lumbar incision was excised Nonfatal complications attributable to this particular technique occurred in 9 patients In eighty-five patients the ureters were completely duplicated Complete ureterectomy was performed in 10 patients and partial ureterectomy in 75 Stumps were removed in 12 patients Difficulties with the blood supply to the remaining ureter made partial heminephrectomy preferable to total Removal of all the ureter at the initial operation seemed to be most valuable when in the female urethra the ectopic orifice was inside the sphincter

A two-stage operation is much safer for it does not compromise the remaining ureter, as it was shown in the 12 patients who were managed in this manner

Endocrine Therapy in Carcinoma of Prostate —Of 1101 patients treated for carcinoma of the prostate, 541 underwent orchiectomy and 560 underwent transurethral resection Endocrine therapy (estrogens or bilateral orchiectomy, or both) and stilbestrol were also used besides surgical treatment A 5-year follow-up study showed a 35 4% survival rate in the nonorchiectomy group without metastasis who received stilbestrol, and a 15 4% rate in the same group who received no stilbestrol In the nonorchiectomy group with metastasis the rate was 21 4% among those who received stilbestrol and there was no survival among those to whom stilbestrol was not given In the orchiectomy group without metastasis the survival rates were 55 8% in the stilbestrol-treated patients and 58 6% among the nonstilbestrol-treated patients The group with metastasis showed a survival rate of 15 % when treated, and a 11 6% rate when not treated with stilbestrol The effect of endocrine treatment for "clinical carcinoma' in patients with metastasis was generally poor, but the survival rates of patients without metastasis were significantly increased by early endocrine therapy Orchiectomy was more effective than stilbestrol

Khirurgiya, Moscow

36 1-152 (March) 1960 Partial Index

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G A Reinberg p 34
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E V Serova and A V Pokrovsky p 69
Diagnosis and Treatment of Obliterating Atherosclerosis
A T Lidsky p 85

Probing of the Patent Ductus Arteriosus —The author's opinion is that in atypical cases of patent ductus arteriosus associated with pulmonary hypertension and blood shunt from right to left, catherization is of slight value for diagnosis In such instances introduction of the probe into the pulmonary artery and the passing of it into the aorta through the patent ductus arteriosus makes the presence of the latter evident The curve traced by the probe during this procedure has a characteristic shape The recording of the pressure curve at the moment of removing the probe from the aorta through the patent ductus arteriosus and into the pulmonary artery permits determination of the amount and direction of the blood escape In 12 of 36 cases the author succeeded in passing the probe through the patent ductus arteriosus

Heart Abdominalization for Coronary Disease —Reinberg believes that the negative pressure of the thoracic frame causes additional work for the heart The additional load is equal to ½ or ⅓ of the total work of the heart This extra load can be avoided by "abdominalization" which consists of an upper coeliotomy and median sagittal incision into the diaphragm of not more than 4 to 5 cm long, after which the pericardium is sutured to the peritoneum As a result of this elliptical opening in the diaphragm, the heart finds itself in a medium with negative internal pressure, very much like the liver, stomach, spleen, and other subdiaphragmatic organs A total of 69 such operations have been performed by various surgeons In 66 cases results were fairly successful, with only 1 terminating fatally

However, the necessity of resorting to laparotomy, and the mortality of 1 5%, make one look for a simpler solution Three new procedures for heart relaxation without laparotomy are suggested (1) conventional left-sided pneumothorax, (2) artificial pneumopericardium, (3) operation on the phrenic nerve to produce paresis or paralysis of the left portion of the diaphragm The 3rd operation may be used at the surgeon's discretion to achieve a temporary effect such as nerve-block, nerve division, injection of alcohol, or freezing with ether chloride, or, to obtain a complete paralysis of the diaphragm exeresis of the nerve may be performed These measures are considered as symptomatic treatment for the most critical cases They should be instituted prior to the cardiac abdominalization proper, and performed by saggittal phrenicotomy They are also useful emergency measures in acute conditions of the heart

New England Journal of Medicine, Boston

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W P Baldus and J B Peter p 700

Illness in a Group of Cleveland Families —This study of the relationship between illness and acquisition of streptococci was limited to 379 acquisitions which occurred in a group of families A control group was selected by matching each person who had acquired a Group A Streptococcus with a person of the same age who had not acquired the organism Types 1, 4, 5, 6, and 12 predominated in the acquisitions of Group A streptococci, although types 2, 11, 13, 19, 28, 31, 33, 41, and 44 were also identified The rate of acquisition was highest among young school children and lowest among preschool children who had no school siblings The rate of streptococcic illness in the acquisition group was 43% while the incidence of "other illnesses in the control group was 29%, which indicates that acquisition of a pathogenic organism by either adult or child produces clinical illness approximately 40% of the time School children, under 6 years of age, were the most common carriers, introducing Group A Streptococcus into the family 6 times as frequently as did their parents Three and 4-year-olds had the highest risk (50%) of becoming secondary carriers Spread of the organism in the family was higher (25%) when the index carrier had a streptococcic illness than when no such illness was developed (9%) It seems desirable to administer penicillin to all members of a family once an initial streptococcic illness is recognized

New England Journal of Medicine, Boston

262 737-786 (April 14) 1960 Partial Index

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Hyponatremia Renal Sodium Loss and Antidiuretic Hormone
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Dietary Fat and Serum Lipids in Diabetes
G J Schroepfer Jr, B Friedrich and F C Goetz p 748
Indole Metabolism in the Malabsorption Syndrome
B J Haverback, B Dyce, and H V Thomas p 754

Hyponatremia and Renal Sodium Loss —In a previous report metabolic studies were presented on 2 patients with broncho genic carcinoma and normal renal and adrenal function The urine was persistently hypertonic to the serum, and body-fluid volume did not contract as sodium depletion and hypotonicity of the serum progressed It was postulated that the underlying process induced inappropriate secretion of antidiuretic hormone and that the syndrome was a consequence of the resulting expansion of body-fluid volume This paper is concerned with metabolic studies in a 3rd patient with bronchogenic carcinoma The hyponatremia in this 60-year old man resulted both from water retention with consequent dilution of body fluids and from an associated loss of sodium in the urine The urine remained hypertonic as serum sodium concentration and tonicity fell to low levels Symptoms of water intoxication, but not of volume depletion, became prominent with reductions of serum sodium and osmolarity Water restriction corrected the electrolyte abnormalities Evidently, continuous inappropriate secretion of antidiuretic hormone is responsible for the hyponatremia Moreover, hyponatremia may occur without sodium loss if salt-retaining hormones are given simultaneously with a water load, which suggests that urinary sodium loss need not be part of the syndrome Treatment of the carcinoma with nitrogen mustard and roentgen irradiation therapy partially corrected the defect in water and sodium metabolism A similar defect in electrolyte and water metabolism has been shown to occur with cerebral damage, and it is possible that the asymptomatic hyponatremia' of pulmonary tuberculosis and meningitis is of similar etiology

New England Journal of Medicine, Boston

262 839 894 (April 28) 1960 Partial Index

Spondylosis Cervicalis and Injury of Cervical Spine
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Infections of Bones and Joints in Children
T S Morse and C V Pryles p 846
Induced Fibrillatory Arrest in Open Heart Surgery
W W L Glenn and others p 852
Asian Influenza Persistent Antibodies Revaccination
W P Boger H G Aaronson and J W Frankel p 856
Acute Myocardial Infarction Secondary to Ergot Therapy
J D Goldfischer p 860

Asian Influenza —The authors report studies on vaccination against Asian influenza which were carried out in the large closed population of the Norristown State Hospital in Norristown, Pa The vaccination of 1,032 patients with commercially available polyvalent influenza-virus vaccines obtained from 6 manufacturers indicated little or no difference in the preparations, from the standpoint of side-effects and a surprising paucity of either systemic or local reactions to the vaccines was noted A group of 229 persons aged 15 to 86 years was treated with some of these vaccines resulting in a fivefold to sevenfold increase of the geometric mean of hemagglutination-inhibiting antibody titers after the subcutaneous injection of 200 to 400 chicken-cell-agglutinating (C C A) units of Asian influenza virus contained as a component of the polyvalent influenza-virus vaccines The intradermal injection of 0 1 cc of a polyvalent vaccine containing only 20 C C A units of Asian influenza virus failed to produce a significant increase in the titers Even though the hemagglutination-inhibiting antibody titers declined shortly after immunization demonstrable residual titers of 1 2 or greater were found in 87% of the 229 persons 12 months after vaccination The titers of older persons were maintained at a higher level than those of younger persons This finding tends to substantiate previously published results indicating a better antigenic response in older than in younger persons to the same antigenic stimulus Revaccination with 20 C C A units of Asian influenza virus contained in polyvalent vaccine administered intradermally in a volume of 0 1 cc is an inadequate antigenic stimulus

Myocardial Infarction Secondary to Ergot Therapy —The author reports on a 35-year-old woman with an 18-year history of classic migraine who for the last 8 years had received ergot derivatives with complete relief of her headaches and without any adverse side-effects She was admitted to hospital because of a severe pressing retrosternal pain, radiating to both shoulders and down both arms, of 30 minutes duration The onset of this pain had occurred about 20 minutes after the intramuscular administration of 0 5 mg of ergotamine tartrate for a severe migraine headache which had proved refractory to the oral administration of 2 mg of ergotamine tartrate An electrocardiogram obtained on the day after admission showed loss of the R wave in leads V through V_3, without significant ST-segment or T wave abnormalities The patient was given meperidine for the relief of pain and large doses of sedatives, and was placed at complete bed rest Although the electrocardiographic changes were not striking, there was recent myocardial necrosis, as evidenced by rise in temperature to a maximum of 101 F (38 5 C), leukocytosis, and a rise of the erythrocyte sedimentation rate and of the serum glutamic oxalacetic transaminase (SGO-T) level to 76 units After these abnormalities had stabilized, there was another attack of chest pain, soon followed by a precordial friction rub, sharply inverted T waves in the electrocardiogram, and renewed rise of the SGO-T level The patient recovered and was discharged from the hospital on the 28th day Apparently, the initial episode of myocardial necrosis was caused by marked coronary-artery vasoconstriction due to the direct action of the ergot preparation on the vascular musculature The subsequent vascular stasis and thrombosis proceeded at a slow enough pace to cause further myocardial damage some days later The author s case is the 1st in which neither an obvious overdosage nor a contraindication to its use could be inferred

New Zealand Medical Journal, Wellington

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D Robb p 97

A Doctor s Approach to the Alcoholic Patient —Excessive drinkers can be divided into heavy drinkers and alcoholics The heavy drinker can stop drinking if it seems necessary to him the alcoholic cannot *control* his *drinking* Loss of control means that after ingestion of any *small quantity* of alcohol a physical demand for that substance is set up which usually ceases only when advanced intoxication makes further intake impossible Control *is never regained* If the alcoholic continues to drink the disease progresses to early death or insanity But though there is no cure, the alcoholic can be helped to stay well Unless he is convinced that he suffers from alcoholism he will not stop drinking With hospitalisation there is usually a rapid improvement in the alcoholic's physical condition As he feels better, he is apt to think that the reason he has not been able to control his drinking is because he was run down physically and now that he is better things will be different What he must learn is that he has already lost the fight An admission of complete defeat in relation to drink is an essential step in an alcoholic's recovery This is the 1st of the 12 steps of the A A program Unless the alcoholic takes this step he cannot really move on to the others He has to be convinced that he cannot regain his health on his own, but that with help he can do so

If the alcoholic can truly accept the presence of a power greater than himself, *he modifies his deepest inner structure, and when he does so without resentment or struggle he becomes serene and contented If he can sustain that inner feeling of acceptance he will remain sober*

Nordisk medicin, Stockholm

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Dynamic Intraosseous Phlebography—Intraosseous phlebography has not developed into a standard procedure The method gives information concerning the presence of incompetent perforating veins in the lower leg and the function of the valves in the deep vein trunks According to the authors' experiences, based on about 359 intraosseous phlebographies, the examination can be carried out under local anesthesia with but slight discomfort for the patient Ambulant application of the method is practicable No instance of iodine hypersensitivity, osteomyelitis, or bone necrosis has been seen Complications occurred in only 2 cases (ulceration of the skin after back-flow of the contrast medium) and can be avoided by careful technique

Revista española de pediatría, Saragossa

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Small Cardioesophageal Malformations
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Thrombosis of Carotid Artery in 14-Year-Old Girl—Thrombosis of the internal carotid artery is extremely rare in children A girl, 14 years old, with paralysis of the left limbs was brought to the Provincial Hospital, Santiago de Compostela, for treatment Six months before consultation the patient had had acute streptococcic tonsillitis complicated by nephritis, convulsions, and paralysis of the left limbs that had lasted for 4 months A diagnosis of thrombosis of the internal carotid artery was confirmed by the results of cerebral arteriography and electroencephalography The thrombus was lodged near the bifurcation of the artery A thrombectomy was performed The postoperative treatment consisted of anticoagulants, vasodilating drugs, and vitamin B_6 The immediate and late postoperative course was uneventful Follow-up for 2 months after the operation showed improvement in the general condition of the patient The functioning of the left limbs improved very slightly, and the electroencephalogram indicated a slight improvement

Revista paulista de medicina, São Paulo

56 95-170 (Feb) 1960 Partial Index

Tuberculous Cystic Cavities of Lungs
A C C Côrtes, R Queiroz, and others p 106
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J de Andrade Sobrinho p 111

Drainage of Thyroid Lymph Nodes in Vivo—The question of whether only the lymphatic juxtathyroid chain should be removed, or whether a radical cervical resection should be performed in thyroid cancer is still unsolved The author attempted to standardize a technique applicable to the surgical treatment of thyroid cancer in orienting the degree of resection The preliminary study consisted of injecting a stain into the thyroid gland of patients scheduled to be operated on for cancer other than that of the thyroid, and which involved cervical dissection Pontamine Sky Blue 5 BX, combined with hyaluronidase in a 4% solution of bi-distilled water, was injected at the beginning of the operation, after the skin flaps had been lifted The resection was performed after an interval of 10 or 15 minutes, during which the lymphatics should have become stained The clinical study was made on 14 patients who received an injection for staining of the caroticojugular, internal jugular, and spinal lymphatic chains The lymph nodes of the internal jugular and spinal chains were stained in 13 of the patients undergoing bilateral cervical resection This finding indicates that the lymphatic chains should be considered as a primary lymphatic station of lymphatic flow from the thyroid Therefore a radical, rather than a partial, removal is indicated in the surgical treatment of thyroid cancer

Semaine hôpitaux de Paris, Paris

36 667-724 (March 4) 1960 Partial Index

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Absolute Prophylaxis of Diabetes
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Hypopituitarism and Diabetes Mellitus—The records of 3 groups of patients were analyzed The 1st group was composed of 7 acromegalic patients whose diabetes disappeared suddenly in consequence of pituitary-vascular accident The 2nd group was composed of 26 diabetic patients in whom hypopituitarism occurred more or less rapidly The disappearance of diabetes mellitus was the 1st sign of hypophysial necrosis in 18 patients, 12 of these died within periods of a few days to 2 months Hypoglycemia was the cause of death in 6 patients and hypopituitarism in 2 The 3rd group was composed of 4 patients in whom diabetes occurred after hypopituitarism had been treated for some time The diabetes occurred spontaneously, was caused by cortisone therapy, or was aggravated by radiotherapy of the pituitary In any of the 3 types of diabetes-hypopituitarism association a characteristic aspect was tolerance to glucides and hypersensitivity to insulin This hypersentitivity can be corrected by a substitutive cortisone treatment Detection of the type of hypopituitarism in diabetic patients is important for diagnostic and therapeutic purposes An acute, undetected hypopituitarism may be the cause of certain irreversible hypoglycemias, the mechanism of which has been unknown until recently

WASHINGTON NEWS

Health Legislation
Project Hope
Radioactivity
Democratic Platform . .

DEMOCRATS PUSH FORAND-TYPE HEALTH PLAN

Democratic leaders put social security health care for the aged high on their list of legislation for consideration by Congress in the short post-convention session

Sen John F Kennedy of Massachusetts, the Democratic nominee for president, told a news conference that we hope that we can pass a bill in the Senate as close as possible to the Forand bill," which the House had rejected before approving the Mills plan financed by federal-state contributions outside the social security system

Kennedy also listed minimum-wage and farm legislation as other measures the Democrats would push in a session expected to last about three weeks With the Senate reconvening on Aug 8 and the House on Aug 15, final adjournment is expected about Sept 1 to permit campaigning for the November elections

Kennedy said that the Democratic platform adopted at the Los Angeles convention had committed the party on legislation, including the social security approach to health care of the aged He said that he believed the Senate Democrats would 'do the best we can' to carry out in the short session the platform's major legislative commitments

However, Senate passage of Forand-type legislation would not mean that it necessarily would become law Any plan approved by the Senate would have to go back to the House The usual procedure on such controversial legislation is for it then to be sent to a House-Senate conference committee for adjustment of differences between the House and Senate versions But an objection from the House floor to this procedure would put the future course of the legislation up to the conservative House Rules Committee

Even if the House should approve a social security health plan, President Eisenhower has indicated he would veto it

One of the first matters on the Senate Finance Committee's schedule after reconvening is a vote on health-care-for-the-aged legislation The Senate Committee held brief hearings on the Mills plan, a section in an omnibus social security and welfare bill, before recessing for the political conventions

Also before the Finance Committee are eight alternative proposals Six of them, all sponsored by Democrats, embody the social security approach Kennedy introduced one of them and was a co-sponsor of a second Senate Democratic Leader Lyndon B Johnson of Texas, the party's nominee for vice-president, reportedly was inclined to favor the plan introduced recently by Sen Clinton P Anderson (D, N Mex)

The Anderson plan would increase social security taxes to provide hospitalization, nursing home care, and visiting nurses services for about 9 million social security beneficiaries aged 68 years or over It has a $75-deductible provision for hospitalization

It appeared probable that any plan approved by the Democratic-controlled Senate would also provide for the aged not covered by social security The Democratic platform states that "we shall provide corresponding benefits" for the aged not covered by social security out of appropriations from the general revenue

The American Medical Association urged the Platform Committee of the Republican National Convention to adopt a health-care-for-the-aged plank "based on the principle that the Federal government should help only those who need help, as determined locally, should be responsive to the needs of the individual and the community through local administration, and should supplement, rather than supplant, state local and private action"

'The A M A is entirely in favor of helping those who need help," Dr Leonard W Larson of Bismarck, N D, President-Elect of the A M A, told the GOP platform committee in Chicago "But the Association does not believe this necessitates the creation of massive federal machinery to help those who neither need nor want help, and who are capable of handling their own problems at the present time"

He said there are dozens of reasons for rejecting any program calling for an increase in social security taxes to finance health care for the aged Listing a few of them, he said

'It would be unpredictably costly, it would unnecessarily cover millions of people, it would substitute service benefits for cash benefits, it would lead to a poorer—not better—quality of medical care, it would overcrowd our hospitals, it would lead to the decline, if not the demise, of private health insurance, it is the outright socialization of the financing of medical care, limited only temporarily to the aged segment of our population, and it would interfere dangerously with the doctor-patient relationship, which is the solid foundation upon which all effective medical care must be based'

HOSPITAL SHIP HOPE ABOUT READY

The Hospital Ship Hope, a floating medical training center sponsored privately under President Eisenhower's People-to-People program, is scheduled to sail Sept 28 from the West Coast for Indonesia, where it is expected to stay for about six months and then go to Viet Nam for another four-months' stay before returning to the United States Dr Mark S Beaubien, aged 38, of Birmingham, Mich, recently flew to Jakarta to set up the ship's visit in Indonesia Project Hope, headed by Dr William B Walsh of Washington, D C, has been conducting a campaign for $3,500,000 in cash and supplies to finance the first operation of the converted Navy hospital ship

Going to a country only on invitation of its medical profession and approval of its government, the "Hope" will have as its main purpose the teaching of American medical and dental skills to doctors, nurses, and technicians at various ports of call It also will carry on research in leprosy and unusual tropical diseases

The government spent about $2 million in foreign aid funds to refurbish the ship which had been in mothballs since World War II Otherwise, the venture is being supported by privately donated money and supplies Hospital beds were reduced from 800 to 230, the extra space being used for teaching rooms and facilities More than 1,000 women applied for the 22 nursing positions aboard the ship

RADIOACTIVITY REMAINS BELOW DANGER POINT

The U S Public Health Service said the latest information available indicates that the levels of radioactivity to which Americans are exposed remain "well below" the danger point

The service issued a bulky report on the levels of strontium 90 and other radioactive substances in milk, air, and water St Louis, Mo, had the highest amount of strontium 90 in milk for the year ending last March 1, according to the data It was followed by Atlanta, Spokane, Wash, and Cincinnati, Ohio, with Overton, Nev, registering the lowest levels for any of the 13 stations in the PHS milk monitoring system

The report also contained preliminary and inconclusive data on a study of strontium 90 content in human bones collected from the St Louis area The service said the number of samples analyzed so far is "too small to permit drawing firm conclusions" It added that the strontium 90 content of bones in the St Louis area does not appear to vary markedly from a previously reported sample collected in other parts of the country

Strontium 90 is the deadliest of all known products of radioactive fall-out and is thought to be a cause of bone cancer

The service also reported a temporary increase in radioactivity after the French nuclear explosion in the Sahara Desert last Feb 13, which lasted through March

DEMOCRATIC PLATFORM ATTACKED

Americans for Constitutional Action charged that the 1960 Democratic campaign platform, which included a social security health care plan for the aged, pointed the way to the final stages of a collectivist state

Retired Admiral Ben Moreell, head of the nonpartisan political action group, said the platform adopted by the Democratic convention in Los Angeles showed "the shocking fact that apparently many of the delegates have been deceived into believing that big centralized, paternalistic, unlimited government can dispense prosperity, health, happiness, security, and even moral strength, to all by some political magic"

Former President Herbert Hoover and Edgar Eisenhower, a brother of President Eisenhower, are trustees of the organization

The U S Chamber of Commerce also attacked the Democrats' health-care-for-the-aged plank The Chamber warned that "once a Forand-type proposal is initiated," it will lead inevitably to complete and compulsory health care for everyone regardless of age This is the real "goal of labor leaders," the Chamber said

MISCELLANY

President Eisenhower signed into law legislation allowing the Food and Drug Administration to set tolerances for chemical additives used in foods and cosmetics Under previous law, any additive that caused damage when tested in large quantities on animals was prohibited, even though small amounts in products such as lipstick would not result in any harm to humans Coal-tar dyes used in most lipsticks were mainly affected The measure continues the government's policy of allowing no tolerances for chemicals found to produce cancer The Administration contended that too little is known about cancer-causing properties to allow any tolerance for such additives

The Food and Drug Administration proposed that vitamin preparations containing high levels of folic acid be sold only on prescription The agency said folic acid is considered harmless by medical authorities, but that it has been known to hide the symptoms of pernicious anemia when taken in large quantities, thereby interfering with correct diagnosis of the disease Folic acid is frequently prescribed for pregnant women The proposed regulation would require a prescription for preparations containing more than four-tenths of a milligram or 400 micrograms per daily dose Manufacturers were given 15 days to comment on the proposal Meantime, over-the-counter sales of vitamin preparations containing less than four-tenths of a milligram of folic acid will be permitted until March, 1961 Unless manufacturers proved by that date that compounds with folic acid are safe as specific levels, doses of preparations containing any amount of the acid would be permitted only by prescription

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Nilevar has been established as a valuable agent[1] for producing gain in weight and increases in appetite, muscle mass and strength in patients with such specific debilitating injuries and diseases as diabetes mellitus, hip fracture, osteomyelitis, osteoporosis, ileitis and rheumatoid arthritis

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Kory and his associates[2] assessed the protein-building effects of Nilevar in fifty-six underweight adults "Statistically significant gains in weight were observed in all groups receiving norethandrolone [Nilevar] these usually were accompanied by increases in appetite and sense of well-being The average weight gain was two pounds per month The maximum was 20 pounds in six months No patient exhibited edema or other signs of fluid retention"

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Nilevar (brand of norethandrolone) is supplied as tablets of 10 mg, drops of 0 25 mg per drop and ampuls of 25 mg in 1 cc of sesame oil with benzyl alcohol

1 Carter, A C Weisenfeld S and Goldner M G Proc Soc Exper Biol & Med 98 593 (July) 1958 2 Kory, R C Watson R N Bradley M H, and Peters, B J J Clin Invest 36 907 (June, part 1) 1957

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MEETINGS

AMERICAN MEDICAL ASSOCIATION Dr F J L *Blasingame*, 535 North Dearborn St, *Chicago 10, Executive Vice-President*

1960 Clinical Meeting, Washington, D C, Nov 28-Dec 1
1961 Annual Meeting, New York City, June 26-30
1961 Clinical Meeting, Denver, Nov 27-30
1962 Annual Meeting, Chicago, June 11-15
1962 Clinical Meeting, Los Angeles, Nov 26-29
1963 Annual Meeting, Atlantic City

AMERICAN

1960

August

American Association of Blood Banks, Jack Tar Hotel San Francisco Aug 21-26 For information write AABB Central Office Suite 1619 30 N Michigan, Chicago 2

American Congress of Physical *Medicine and Rehabilitation*, Mayflower Hotel Washington, D C, Aug 21-26 Mrs Dorothea C Augustin 30 N Michigan Ave *Chicago 2 Executive Secretary*

American Hospital *Association*, Civic Auditorium, San Francisco, Aug 27-Sept 1 Mr Maurice J Norby, 840 N Lake Shore Dr, *Chicago 11* Secretary

American Institute of Ultrasonics in Medicine Statler-Hilton Hotel Washington D C Aug 20 Dr Dorothy M Stillwell, *Dept of Phys* Med and Rehab, Univ *of Colorado Med Center, Denver 20* Chairman

American Physiological *Society Stanford University*, Calif Aug 22-26 Mr Ray C Daggs 9650 Wisconsin Ave, *Washington 14 D C* Executive Secretary

American Society of Clinical Hypnosis Miami, Fla, Aug 7-10 Dr Seymour Hershman, 6770 N Lincoln Ave Chicago 46, Secretary

American *Society* for Pharmacology and Experimental Therapeutics, University of Washington, Seattle Aug 21-25 Dr Karl H Beyer Merck Sharp & Dohme Research Laboratories, West Point Pa Secretary

American Veterinary Medical Association *Denver-Hilton Hotel* Denver Aug 15-18 *H E* Kingman Jr 600 S Michigan Avenue, Chicago 5 Executive Secretary

Biological Photographic Association, Inc, Utah Motor Lodge Salt Lake City Utah, Aug 23-26 *Miss Jane H Waters*, Box 1668 Grand *Central* P O, New York 17, Executive Secretary

Conference on the Chemical Organization of Cells Normal and Abnormal, University of Wisconsin Madison, Aug 25-27 Dr J F A McManus, Dept of Pathology, University of Alabama Medical Center, Birmingham, Chairman

Gerontological Society Inc, Mark Hopkins Hotel, San Francisco, Aug 7-12 Mrs Marjorie *Adler* 660 *S* Kingshighway Blvd St Louis 10 Administrative Secretary

National Medical Association Inc Penn-Sheraton Hotel, Pittsburgh Aug 8-11 Dr John T Givens, 1108 Church St, Norfolk Va, Executive Secretary

Reno Surgical Society, Mapes Hotel, Reno Nev Aug 18-20 Dr Gilbert G Lenz, 505 S Arlington Ave, Reno, Nevada

Rocky Mountain Radiological Society, Denver-Hilton Hotel Denver Aug 11-13 Dr John H Freed, 4200 E 9th Ave, Denver 20 Secretary-*Treasurer*

St *Joseph's Hospital* Annual Clinics, St Joseph's *Hospital Denver* Aug 3-5 Dr W H Leitch, St Joseph's Hospital, 1818 Humboldt St *Denver* 18 Chairman

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs Aug 25-27 Mr Charles Lively Box 1031 Charleston 24, W Va, Executive *Secretary*

September

American Academy of Pediatrics, and American Academy of General Practice, *Louisiana Chapter, Roosevelt Hotel*, New Orleans Sept 23 Dr Herbert B Rothschild, 1520 Louisiana Ave, New Orleans 15, Chairman of Publicity Committee

American Medical Writers' Association, Hotel Morrison, Chicago, Sept 30-Oct 1 Dr Harold Swanberg, 510 Maine St, Quincy, Ill, Secretary

American Roentgen Ray Society, Ambassador Hotel Atlantic City Sept 27-30 Mr Hugh Jones 20 N Wacker Dr, Chicago 6, Director, Public Relations

American Society of Clinical Pathologists, *Palmer House*, Chicago Sept 24-Oct 2 Mr Claude E Wells, 445 Lake Shore Drive, Chicago 11, Executive Secretary

College of American Pathologists Palmer House, Chicago, Sept 24-27 Dr Arthur H Dearing, 2115 Prudential Plaza, Chicago, Executive Director

Colorado State Medical Society, Stanley Hotel, Estes Park, Sept 14-17 Mr Harvey T Sethman, 835 Republic Bldg, Denver 2, Executive Secretary

Delaware, Medical Society of, Rehoboth, Del, Sept Mr Lawrence C Morris Jr, 1925 Lovering Ave, Wilmington 6, Del, Executive Secretary

Flying Physicians Association, third clinical *meeting*, Western Hills Lodge, Wagoner, Okla, Sept 6-9 For information write Flying Physicians Association National Headquarters, P O Box 3275, Tulsa, Okla

Inter-Society Cytology Council, Palmer House, Chicago, Sept 23-25 Dr Paul A Younge, 1101 Beacon St, *Brookline 46, Mass*, Secretary

Kentucky *State* Medical Association, Louisville, Sept 20-22 Mr J P Sanford, 1169 Eastern Parkway Louisville 17, Ky Executive Secretary

Maryland, Medical and Chirurgical Faculty of the State of *Semiannual Meeting Ocean City, Sept 16* Mr John Sargeant 1211 Cathedral St, Baltimore 1, Executive *Secretary*

Michigan State Medical Society, Detroit, week *of* Sept 25 Dr D Bruce Wiley 606 Townsend St, Lansing 15, Mich, Secretary

Montana Medical *Association*, Baxter Hotel Bozeman Sept 15 Dr William E Harris, 114 N *Second*, Livingston, Montana Secretary

National Cancer Conference, American Cancer Society, Inc and the National Cancer *Institute*, Minneapolis, Minnesota Sept 13-15 Dr Roald M Grant 521 W *57th St, New York 19*, Coordinator

National Recreation Congress *Shoreham* Hotel, Washington D C Sept 25-29 Willard B Stone 8 W Eighth St New York 11, Secretary

Nevada State Medical Association, Stardust Hotel Las Vegas Sept 7-10 Mr Nelson B *Neff*, P O *Box* 2790, Reno Nev Executive Secretary

New England *Society of Anesthesiologists Bretton Woods* N H *Sept* 18-19 *Dr* Thomas K Burnap P O Box 81, Kenmore Station P O, Boston 15

Oregon State Medical *Society Portland* Sept 7-9 Mr Roscoe K Miller, 2164 S W Park Place, Portland 5, Ore, Executive *Secretary*

Pacific Dermatologic Association, Empress *Hotel*, Victoria, British *Columbia Canada, Sept 1-4 Dr* Edward J Ringrose, 2636 Telegraph Ave Berkeley 4, Calif, Secretary-Treasurer

Society for Pediatric Radiology Ambassador Hotel Atlantic City N J *Sept 26 Dr* Richard C *Lester* 412 *Union St* S E Minneapolis 14 Minn, Secretary-Treasurer

Southern Trudeau Society (and Southern Tuberculosis Conference), *Hotel* Francis Marion Charleston S C, *Sept* 14-16 Mr Judson M Allred Jr P O *Box 9865 Northside Station*, Jackson Miss, Secretary-Treasurer

Tennessee Valley Medical Assembly Read House, Chattanooga Tenn *Sept* 26-27 Dr *Robert A Waters* 109 Medical Arts Bldg Chattanooga Chairman

Tri-State Medical Assembly, Captain Shreve Hotel, Shreveport, La *Sept* 14-15 Dr J W Wilson Jr, 940 Margaret Place Shreveport, La, Secretary-Treasurer

Utah State Medical Association, *Hotel* Utah Motor Lodge Salt Lake City *Sept 20-23* Mr *Harold Bowman* 42 S 5th East, Salt Lake City 2 Executive Secretary

Washington State Medical Association, Seattle Sept 25-28 Mr Ralph W Neill, 1309 Seventh Ave Seattle 1, Executive Secretary

Wyoming State Medical Society Jackson Lake Lodge Moran Sept 7-10 Mr Arthur R Abbey, P O Box 2036, Cheyenne, Wyo, Executive *Secretary*

October

Academy of Psychosomatic Medicine, *Benjamin Franklin Hotel*, Philadelphia, *Oct* 13-15 For information write Dr Bertram B Moss, 55 E Washington Chicago 2

American Academy for Cerebral Palsy, Penn-Sheraton Hotel Pittsburgh, Oct 5-8 Dr Joseph D Russ 1520 Louisiana Ave, *New Orleans* 15 Executive Secretary

American Academy of Ophthalmology & *Otolaryngology*, Palmer House Chicago, Oct 9-14 Dr William L *Benedict 15 Second St* S W Rochester Minn, Executive Secretary

American Academy of Pediatrics Palmer House *Chicago Oct 17-20* Dr E H Christopherson 1801 Hinman Ave, Evanston Ill, Executive Director

American Association of Medical Clinics *New Orleans Oct 6-8 Dr* Joseph B Davis 134 N Washington St, Marion Ind, Secretary

American Association of Medical Record Librarians Olympia Hotel Seattle *Oct* 10-13 Miss *Doris* Cleason, 840 N Lake *Shore Dr* Chicago 11 Executive Director

American Association of Poison Control Centers, Palmer House Chicago, *Oct* 18 *Dr* Harry *C Shirkey* 712 *S 30th St* Birmingham, Ala Chairman Program Committee

American Association for the Surgery of Trauma Coronado Hotel Coronado, Calif Oct 5-7 Dr William T Fitts Jr, *3400 Spruce St*, Philadelphia 4, Secretary

American College of Gastroenterology, Bellevue Stratford Hotel Philadelphia, Oct 23-26 Mr Daniel Weiss, 33 W *60th St*, New York 23, Executive Director

American College of Surgeons, Clinical Congress, San *Francisco*, Oct 10-14 For information write Dr William E Adams, 40 E Erie *St*, *Chicago 11*

American Fracture Association, El *Presidentia Hotel* Mexico D F Mexico, Oct 30-Nov 4 Dr H W Wellmerling, 610 Griesheim Bldg *Bloomington, Ill*, *Executive Secretary*

American Heart Association Inc, Jefferson Hotel, St Louis Oct 21-25 Mr Rome A Betts 44 E 23rd St New York 10 Executive Director

American Otorhinologic Society for Plastic Surgery, Inc, Conrad Hilton Chicago Oct 9 Dr Joseph G Gilbert, 75 Barberry Lane Roslyn Heights L I New York, Secretary

American Public Health Association, *San Francisco* Oct 30 Nov 4 Dr Berwyn F Mattison, 1790 Broadway, New York 19, Executive Director

American Rhinologic Society Belmont Hotel, Chicago, Oct 8 Dr Robert M Hansen, 1735 N Wheeler Ave Portland 17, Ore, *Secretary*

American School Health Association, San Francisco, Oct 30 Nov 4 Dr A O DeWeese, 515 E Main St, Kent, Ohio, *Executive Secretary*

American Society of Anesthesiologists, Inc, Statler Hilton New York City Oct 2-7 Mr John W Andes 515 Busse Hwy, Park *Ridge* Ill, *Executive Secretary*

American Society of Facial Plastic Surgery, Chicago, Oct 13, Dr Samuel M Bloom, 123 E 83d St, New York 28, Secretary

American Society of Plastic and Reconstructive *Surgery*, Statler Hotel, Los Angeles, Oct 2-7 Dr *Thomas* R Broadbent, 508 E S Temple, Salt Lake City, Secretary

Association of American Medical Colleges, Diplomat *Hotel Hollywood* Beach Fla, Oct 31-Nov 2 Dr Ward Darley 2530 Ridge Ave, *Evanston*, Ill Executive Director

(Continued on page 28)

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JULY 30, 1960

LASTING IDEALS OF ABRAHAM FLEXNER

Lewis L Strauss, Washington, D C

BECAUSE ideals are come by early, it is profitable to look at the circumstances of a man's boyhood and youth when that insight is available Abraham Flexner left a revealing and delightfully written account of that early period in his career He was born in a small Kentucky community, the sixth of nine children, to Jewish parents who had met and married in the United States but who had arrived as immigrants from Europe during the 1850's His father died before Abraham was 16 years old, but his precept and example left indelible impressions on the growing boy Although both parents had only limited formal educations, they shared a tremendous respect for culture and made prodigious sacrifices to see that their children received every cultural advantage that the locality afforded

The father had been successful in business almost from his arrival and until 1873, but he lost what he had accumulated in the panic of that year Speaking of that period, Flexner had written as follows "I am still at a loss to understand the courage and confidence with which my parents contemplated the future of their large family I do not recall a single word of complaint They did not bemoan their fate, never a word of bitterness or envy escaped either It made no difference to them that others were more fortunate or successful They had pitched their own ideals incredibly high and no pressure of external circumstances, no temporary expedient to which they had to resort, such as putting the older boys to work to help support the family, ever lowered their aims even for the time being, nor did they lean on others I marvel as I look back at their confidence and serenity What spiritual force sustained them they faced facts, endured, clung to ideals and acted fearlessly, persistently, confidently"

This is typical of his description of his parents, a blend of affection and profound filial respect Describing them, Flexner quoted the following from the poet, Vergil "Possunt, quia posse videntur' (They could because they thought they could) This was the environment in which the ideals of Abraham Flexner were formed

In Louisville in those days, there were a number of families with pronounced intellectual leanings, among them the Brandeis family and others who had come over from Europe in 1848, 1849, and subsequently Some of them lost sons and fathers in the War between the States, which occurred shortly afterwards When Flexner was a boy, these families sought to forget the past and its hardships and plunged enthusiastically into the literary and scholastic pursuits of the day

The youthful Flexner passed through the classrooms of an extraordinary series of teachers, a fact which he always regarded as an unusual piece of good fortune From each of them he imbibed some truth and principle as well as the Latin and Greek which were indispensable in those days to the man desiring a well-rounded education He was also exposed to science in the lectures of Prof Thomas W Tobin, but the exposure did not take' He attended the lectures assiduously, kept notes, and was awarded a prize for 'having made the most adequate notes on the lectures It was a copy of Webster's dictionary, and he kept it all his life "It is the one and only trophy I have ever received in the field of science," he once wrote "The other contestants must have been dull indeed for I do not believe that I understood the lectures then and

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Part 2 in a symposium of papers read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 8 1960 Part 1 of the symposium was published in the July 23 issue of The Journal

I am certain that I do not recall their substance now"

"From my 15th year on," he said, "I was continuously in contact with mature persons who were infinitely my superiors" At home, certainly, he was continuously in the atmosphere of a parental example in which only the best and most excellent was acceptable as an ideal for any endeavor Saluting the memory of his father, he said, "His ideals were his legacy—his only legacy—to his family"

Writing about the South of 1890, at which time he was 24 years old, Flexner made the following observation "We are told by latter-day economists and publicists that the frontier disappeared in 1890 and that from that date a new order became inevitable Well, it did not disappear with a crash as did the social system in the South There are some people for whom there never was a frontier and others for whom the frontier still exists There still exists that moral and intellectual frontier which has persisted through the ages Are not thrift, family solidarity, self-help and self-denial just as valuable assets in our day as they were in the days of our fathers?"

In his later years, concerned about the future of his children, nephews, and nieces, he observed in a letter to his brother Simon that the children would be superior in culture and intelligence "But," he asked, "will their fiber be as tough? Will they try to get as far beyond their point of origin as we tried to get beyond ours? Will they have the earnestness and the ambition? That is the question"

And years later he answered it in part "It cannot come about," he said, "by the paternal oversight of the Federal Government" Thus we see that the seeds of the ideal of individual independence and hard work were deeply planted

He had plenty of hard work as a student at Johns Hopkins, of which the great Daniel Coit Gilman had become president when the university was founded in 1876 In 1884, at the age of 17 years, Flexner entered college He graduated in 1886, only two years later That was not due solely to precocity but also to the length of the course In those days there were no secret societies, fraternities, organized athletics, or Class of '86 or Class of '87 But there was a group of students who were eager to learn, a "picked group" Writing of this period, Flexner has said, "I contend that all colleges should contain 'picked groups' and that boys and girls not qualified by their intellectual ability or their seriousness of purpose to enter a picked group should procure in some other kind of institution such technical or other instruction and discipline as they may require or desire" This was the beginning of the Flexner ideal of educational excellence There also began his lifelong admiration for Gilman

Flexner was concerned lest Gilman's great contribution to education be forgotten "Educational processes and systems," he said, "are usually of evolutionary origin Three centuries of gradual development are responsible for present-day elementary, secondary and college systems But the graduate school, research institutes, and medical schools now flourishing in the United States are not the slow outcome of evolution, they represent an unprecedented leap in the dark, with none of the gradual intervening stages characteristic of evolutionary change Mr Gilman took this leap The Johns Hopkins University was an outright innovation, the ground had not been prepared for it Yet so complete and rapid was its success that within two decades its own graduates reproduced it in a considerable number of American institutions of learning A single generation of scholars thus displaced evolutionary growth that might otherwise have required a century or more" This was Flexner's justification for the picked group Constructive innovation in education became another of his ideals

At the age of 74, he spoke as follows on the subject of preparing teachers "I am no friend of teachers' colleges in the form that they have now assumed They are absurd institutions, making no distinctions between what is significant and what is insignificant, admitting huge hordes of persons mostly without background, and usually without scholarly ambition, and undertaking by minute training in methods and statistics to produce a good teacher The bad teaching that is so common in the United States is, in my judgement, in part due to the turn which teachers' colleges have taken in subordinating to training in technique the knowledge of the subject to be taught, and to the wirepulling by which they have persuaded state and city boards of education to exact a certain number of hours of their training before anyone can become a 'qualified' teacher or obtain promotion"

School for Boys

In 1890, in order to make a living and to contribute to the support of his mother, Flexner established a small school in Louisville for boys who had had a disastrous career in other schools—sometimes so disastrous, he recalled, that when a good boy was brought to him, it was not uncommon for people to say, "I thought John was a good boy but now I hear he is going to Mr Flexner's school" His bread and butter depended on his success with problem students, some of them "just plain stupid, others indifferent" Although one became a federal judge and some others gave a good account of themselves in later life, Flexner cared only for excellence He echoed a quotation ascribed to Cambon, "We have to defend the country against mediocrity, mediocrity of soul, mediocrity of ideas, mediocrity of action We must fight against it in ourselves"

"This may sound intolerant," Flexner wrote "Such is not the case Throughout my life I have pursued excellence but I was never indifferent to mediocrity I tried hard to do what I could for it, sometimes with results that were surprisingly good In general, however, I realized early the impossi bility of combining a tender regard for mediocrity with a real enthusiasm for learning"

He used to relate amusing experiences about pupils who were inept in one subject or another He recalled the case of one pupil who was just getting ready to take college entrance examinations when he came down with mumps, lost time from classes, and was worried that he did not know enough about quadratics to pass Flexner comforted him by offering to coach him and, when he resumed his studies, pointed out to him that only three or four types of quadratics ever appeared on an examination paper These he took up one at a time and drilled the boy in solving the equations in the accepted fashion The student mastered this purely mechanical operation and, with restored confidence, thanked Flexner but then, seized with sudden apprehension, inquired, But what is a quadratic? Don't let that worry you," Flexner replied 'That is one question that never appears on a college entrance examination paper" The student took the examination, passed it, and won a scholarship without the slightest idea of what a quadratic was

The cultivation of excellence was the creed and the ideal which Flexner proceeded to implement at the Carnegie Foundation, at the General Education Board, in his Rhodes lectures, and finally and without compromise,' as he put it, in the founding of the Institute for Advanced Study

In practical terms," he said, "the pursuit of excellence merely meant that mediocrity must not set the standard Let us do for it all we can, perhaps even shake it out of itself, but let us not blind ourselves to the fundamental distinction between mediocrity and excellence"

Once, while serving on the Board of Education of New York City, he tried to persuade his colleagues to set aside just one high school for unusual or gifted students A mere handful of his associates voted with him This rejected idea has since materialized, but Flexner's warning that a democracy which fails to appreciate excellence is a democracy in danger went long unheeded

Bulletin Number Four

Flexner's impact on medical education as a result of his famous Bulletin Number Four is historic He made a survey of medical colleges in the United States and Canada in 1909 and visited 155 of them They had grown like mushrooms The account was startling Medical education had degenerated scandalously since the days of its founding in the United States The schools, with few exceptions, were essentially private ventures conducted for profit It had not been many years since a school that was founded in October would graduate a class the next spring The chairs of departments were profitable and were put up for bids as entrance and tuition fees were divided among the holders In many of these schools, no applicant who could pay his tuition was turned down for lack of scholarship In many states, diplomas alone were a license to practice

Some examples of the conditions which Flexner found are interesting In Salem, Ore, he asked the dean of the medical school whether or not the school possessed a physiological laboratory The dean replied, "Surely, I have it upstairs, I will bring it down to you" He went up and brought down a small sphygmograph

On another occasion he visited a school in Des Moines with the dean of the school and found every door locked, although on the outside each bore a name such as anatomy, physiology, and pathology The janitor could not be found, probably not altogether an accident, Flexner supposed, and having expressed his satisfaction Flexner was driven to the railroad station and left, as the dean supposed, to take the next train to Iowa City Instead, after waiting until the dean was out of sight, Flexner returned to the school and found the janitor who, in return for $5, opened every door The equipment in each of the rooms was identical—a desk, a small blackboard, and chairs There were no charts or apparatus

The report contained more shocking findings

In Alabama at Birmington Medical College "A stock company paying annual dividends of 6%, the hospital given over largely to surgical patients with gun-shot and other wounds'

In Arkansas in the Medical Department of the University of Arkansas "City hospital of 30 beds, no ward visits, of postmortems no mention"

In California at California Medical College "Entrance requirements nominal No dispensary The School is a disgrace to the State whose laws permit its existence"

In Georgia at the College of Eclectic Medicine and Surgery "Nothing more disgraceful calling itself a Medical School can be found anywhere'

In Illinois at Northwestern University Medical Department Entrance requirement one year of college work and even that hitherto loosely enforced'

In Kentucky at University of Louisville 'Entrance requirement less than a high school education Examples were found of students admitted from two-year high schools or less"

In Massachusetts at Tufts College Medical School Entrance requirement below an actual high school'

In New York at University of Buffalo Medical Department Despite the University charter, the University of Buffalo is a fiction'

Great Fund Raiser

Flexner's success in raising large sums of money from Andrew Carnegie, John D Rockefeller, J P Morgan, Julius Rosenwald, and other philanthropists of the day is also historic But it was the intelligent use of these sums which corrected conditions like those described and restored the dignity and vitality of medical education in the United States Flexner never made any effort to manage science or education and would have regarded any such suggestion as preposterous His system was to find out who were the worthy leaders, to take their advice, and to help them, giving them what they needed and trusting them absolutely This procedure, based on a discriminating judgment of human nature and individual ability, paid off handsomely

In his later years, Abraham Flexner met Louis Bamberger and Mrs Felix Fuld These were people whose background was similar to his own, save for the fact that they had amassed great fortunes while his labors had never been rewarded with more than a simple living—nor had he ever wanted more The generosity of Mr Bamberger and Mrs Fuld, however, led to the realization of Flexner's great ambition to establish an institution of higher learning and for the encouragement of undoubted excellence His interests had always been pragmatic to teach or to enable someone else to teach intelligently and, above all, selectively This, through his life, was a lasting ideal and, as a great ideal, it survives his physical concern with it

It might be appropriate to conclude by returning to the scenes of his childhood and early youth He spoke often of his mother's aphorisms "I must confess,' he once wrote, "that they seemed to me the sum of earthly wisdom—kindness, gentleness, helpfulness, faith in the ultimate outcome of high endeavor, a willingness to clutch the skirts of circumstance be the circumstance of our own preference or not, and finally the importance throughout life of maintaining an easy attitude

"Have a few friends and, from beginning to end, aim at the prepared mind"

He said he often thought of Carlyle's simple bookplate, which had made a great impression on him when he saw it for the first and only time in the 1880's The bookplate shows a lighted candle beneath which the legend reads, "I burn that I may be of use" The flame of Abraham Flexner's candle will not go out, it will always light the way to excellence

1925 K St, N W (6)

HALLMARKS OF UNIVERSITY EDUCATION

Nils Y Wessell, Ph D, Medford, Mass

I have strong conviction that we need a reminder of what the hallmarks of the university are This is particularly true of those of us who are involved in education for the professions We need to hear repeated those considerations and we need to hear restated those standards and ideals which make the university, and not the guild, the proper repository for professional education's responsibilities

One does not have to be a university teacher or administrator to be committed to any one or all of the fundamental principles which I define as the hallmarks of university education, but it is in the true university alone that you will find all of these principles daily determining the functions and setting the qualitative bench marks through which and by which the university is operated I was careful to use the phrase "true university," in recognition, of course, that compromise with these fundamental principles is not unknown in the real as opposed to the ideal university But no man-made institution with which I am acquainted is perfection in all its parts

Commitment to Intellect

The first of these hallmarks is represented by what Howard Lee Nostrand calls "Western man's determination to live according to his intellect" This is the first article of faith, that man's intelligence properly trained and disciplined can be relied on to make progress toward and to achieve that which is good The good which intellect serves includes the moral, the economic, and the physical The university's commitment to intellect does not mean that emotion, sentiment, and aesthetic experience are of no significance or in time will be eliminated by sheer reason On the contrary, it means that through intellect and the understandings emotion, sentiment, and aesthetics can be enriched Intellect requires passion for its fulfillment I believe that this is what Whitehead had in mind when he said "The justification for a university is that it preserves the connection between knowledge and the zest of life, by inviting the young and the old in the imaginative consideration of learning'

This determination to live by intellect implies the future reference which clearly characterizes the university and which has been aptly stated by Lester Evans when he speaks of the university as the one social institution specifically charged with anticipating the future This responsibility for the future obviously demands the effective use of intellectual skills represented by all of the disciplines that make up a university This statement is not tantamount to saying that man can live by the bread of intellect alone Neither can man live by indulging only in the activities which characterize

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President, Tufts University

Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 8 1960

the teacher and the student in the university. The statement of Nostrand's previously quoted is repeated now in its entirety: "The university is the embodiment of Western man's determination to live according to his intellect."

The determination to live one's life according to his intellect is the difficult option, not the "easy option" of which Barbara Ward speaks in diagnosing our ills as a people, the difficult option which, however, in the long run provides the greater rewards and the more significant pleasures. The first hallmark of the university, then, is that it elects voluntarily as its taskmaster the sternest of all, the intellect.

This high-sounding generalization may seem to ring hollow when we observe the extent to which many a university concerns itself with entertainment rather than with the serious matter of intellect. This is sometimes illustrated in subtle ways in the classroom but most obviously on Saturday afternoons in the fall (from Labor Day to New Years' day). The only question is whether the marching bands or the football squads spend more time and energy each week in the attainment of the skills they exhibit. Nowhere does the university depart further from its primary commitment than in these weekly spectacles in which it officially indulges.

Free Inquiry in the Search for Truth

Other hallmarks of the university derive simply by definition from this first, the commitment to intellect. Foremost among them is the principle of free inquiry in the search for truth. This needs no elaboration for persons who play as much as part in education as do members of the medical profession. Although the university in its individual schools may train students for medicine, law, the ministry, or business, its overriding concern does not have and is not subject to the restrictions of profession or vocation. The university apart from its individual schools and colleges has the complete kind of intellectual freedom which is one of its most important hallmarks. This freedom is also one of the best guarantees that tomorrow's physician or lawyer will be better trained and educated than yesterday's.

If medical education is to mature, as I believe it should, as a university discipline and not as a vocational apprenticeship, then it must follow this tenet of free inquiry. It will be free to follow it only in the university setting. Only the university with its traditions can protect medical education from the professional, political, and social pressures which would result in the loss of this essential freedom. It is this hallmark of the university which clearly makes the distinction between the academy and the guild, whatever profession the guild represents.

President Eliot, Harvard University, in the 1920's applied the principle of free inquiry to the complex university when he said, "The division of subject between the professional schools of a university is deep and wide. The student of medicine hardly touches one of the subjects to which the student of divinity or of law must almost exclusively devote himself, the student of theology pays no attention to a great group of subjects which occupies completely the time of the student of electrical engineering for four years, yet in a true university the spirit of the teaching and of the study in preparation for all these varied professions is one and the same, viz., the spirit of modern science—candid, fearless, truth-seeking, searching for the fact regardless of the consequences." While the intervening decades have reduced considerably the distinctions Mr. Eliot drew in these comparisons, his final generalization, the important one, still holds.

There are medical schools whose university affiliation is prized only because of the "cloak of respectability," to use Dean Lippard's phase, the tie provides. A sentence by Henry S. Pritchett, then president of the Carnegie Foundation for the Advancement of Teaching, in his introduction to Abraham Flexner's report is timely. "A university has a mission greater than the formation of a large student body or the attainment of institutional completeness, namely, the duty of loyalty to the standards of common honesty, of intellectual sincerity, of scientific accuracy."

John Masefield put this in poet's words by saying that wherever a university exists, "the free minds of men, urged on to full and fair enquiry, may still bring wisdom into human affairs" where "seekers and learners . . . will uphold ever the dignity of thought and learning and will exact standards in these things."

Concern for Means and Ends

Masefield makes clear that another hallmark of the university is a concern for means and ends. The ends of education as well as the means to these ends are of first concern to the university. Ends without means promote immorality. Means without ends promote sterility. Adolph Hitler and Joseph Stalin, and even some homegrown American extremists, have illustrated clearly the immorality of ends that ignore means. Our present lack of national purpose illustrates the sterility of a way of life which concerns itself first and foremost with means.

Our present mode of living, as well as that of many other civilizations which have paraded across history's stage and disappeared, has been indicted for being rich in means but without ends or purpose. This reference is primarily directed to material means, the kind of which no university can be said to have a rich supply. On the other hand, the university can be said to be rich in its intellectual treasures. It is these means, these treasures, which the true university does not dissipate because of the absence of purpose. Whitehead certainly had the problem of means and ends in mind when, in a lecture on the aims of education, he said first, "A merely well informed man is the most useless bore on God's earth," and second, "Knowledge does not keep any better than fish."

I do not speak of one of the hallmarks of the university as being a balance between means and ends, for no such balance can honestly exist. The university concerns itself with both means and ends and does not pride itself on a neat and equal weighing of the two. It passes a moral judgment and a qualitative judgment with respect to both.

There are those who would argue with sincerity that *the university should be amoral*, passing judgments as to truth and accuracy but not with respect to morality. Such a stand denies that ends must be measured by means as well as for themselves.

Cultural Synthesis and Unity of Knowledge

Finally, the hallmark of the university is its concern for cultural synthesis and for the unity of knowledge, whether promoted by scholarship, discovery, or invention. It is this emphasis which will prevent the modern professional man from becoming the "new barbarian," whom Ortega describes as "*more learned than ever before*, but at the same time more uncultured—the engineer, the physician, the lawyer, the scientist."

While Eliot in his dedication of the elective system could hardly be considered the father of general education, he was far from ignorant of the importance of cultural unity when he said, "Students of history and natural history, of physics and metaphysics, of literature and the fine arts, find that, though their fields of study are different, their method and spirit are the same. This oneness of method characterizes the true university, and partly justifies the name." By the latter phrase he meant of course that the word university means much in one.

It is this emphasis on synthesis and unity that makes of the university the proper place for training in the professions. It may be that some new science or specialty yet unborn may hold the great promise for medicine, engineering, or some other profession. Or the promise may be found in less dramatic developments such as those in the humanities and the social sciences. The university moves forward on all intellectual fronts. It weighs the *promise of new knowledge* by ends that may at first have no seeming relevance for the practice of a profession. To all these efforts which make these developments possible it applies the same yardstick of *excellence*.

Advancing knowledge can be represented as an expanding circle, the perimeter being the contact with the unknown. As the circle grows with new knowledge so does our contact with the unknown and therefore our appreciation of the vastness of the unknown. The analogy of course breaks down if we think of the circle as expanding in regular fashion, uniformly in each of its quadrants. Such regular expansion of the circle of knowledge obviously does not take place, but the figure of speech illustrates the point that we do not know for sure where most of the promise for any professional field *lies in the future. The university, happily, is concerned* with the whole circle (perhaps only in the *collective sense) and can guarantee that change* will not be bound by preconception and previous custom. The university is the agent by which the adventure of action meets the adventure of thought.

Summary

There are four important hallmarks of university education. The first is a commitment to intellect. By implication this suggests the second, the principle *of free inquiry* in the search for truth. In this process the university, in the third place, is concerned with both ends and means. In the fourth place, it is concerned with the opportunity to demonstrate the possibility of cultural synthesis and the unity of knowledge.

THE MEDICAL SCIENCES—A SOURCE OF SCHOLARLY STRENGTH FOR THE UNIVERSITY

H. Stanley Bennett, M.D., Seattle

A proper affiliation of medical schools with universities, though advocated as a reform measure in the United States by Flexner, is actually of ancient and noble sanction. Eight hundred years ago the Universities of Salerno and Montpelier boasted of eminent doctors in their medical faculties. Faculties of medicine were necessary and standard features of medieval European universities.

Medieval Learning

But medieval universities were primarily instruments for disseminating and fortifying orthodoxy. Once they had assimilated the classical learning of the ancients and reconciled it with Christian dogma, medieval universities continued as essentially teaching institutions, passing on and working over the knowledge of the past, but *contributing* little that was new. Francis Bacon speaks thus of the substance of medieval university curricula: "This kind of degenerate learning did chiefly reign amongst

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Chairman, Department of Anatomy, University of Washington School of Medicine.

Read before the 56th Annual Congress on Medical Education and Licensure, Chicago, Feb. 8, 1960.

the schoolmen, who having sharp and strong wits, and abundance of leisure, and small variety of reading, but their wits being shut up in the cells of a few authors (chiefly Aristotle their dictator) as their persons were shut up in the cells of monasteries and colleges, and knowing little history, either of nature or time, did out of no great quantity of matter and infinite agitation of wit, spin out unto us those laborious webs of learning which are extant in their books For the wit and mind of man, if it work upon matter, which is the contemplation of the creatures of God, worketh according to the stuff and is limited thereby, but if it work upon itself, as the spider worketh its web, then it is endless, and brings forth indeed cobwebs of learning, admirable for the fineness of thread and work, but of no substance or profit"[1] This, my friends, is Bacon's statement of the merits of institutions devoted solely to teaching the learning of the past, as compared to those devoted to teaching and research, where the learning of the past is checked and corrected continually by observation of man and of nature

The basic premise of medieval learning was that knowledge is to be gained primarily by consulting the authorities In several populous countries in the far east, the most effective way to wisdom and learning was deemed to be through meditation Thus, Gautama Buddha and the Bodhisattva, Dharma, achieved enlightenment by prolonged undisturbed thought, little checked by appeals to the literature or observation

Modern learning is based on a premise attributed to Thales of Miletos of the sixth century B C Thales suggested that the best way to learn about something is to study that something itself Modern scholarship recognizes the importance and value of meditation, of thought and of thorough study of the observations and ideas of earlier workers, but the final appeal is to the evidence itself, to observation of nature and the activities of man These principles are now well established in universities, yet it is sobering to contemplate that historically, universities clung all too long to the concept that their function was merely to transmit the knowledge of the past Indeed, in England and the United States, universities were particularly late in achieving the necessary reforms, which became firm policies in these countries only late in the nineteenth century The conservatism of university faculties in many countries caused intellectual leadership to fall by default to learned people outside universities Thus for several centuries in this country, in Great Britain and on the Europeon continent, the main efforts of scientific research and lofty scholarship were carried out by men of means and leisure outside universities, fostered and encouraged by the Royal Societies and Academies Thus Copernicus, Harvey, Boyle, Davy, Faraday, Hunter, Sydenham, Jenner Leeuwenhoek, Lavoisier, Franklin, Priestley, Gilbert and Hooke made their contributions to learning quite independent of universities, and, in many cases, largely ignored by contemporary university dons

Medical faculties in medieval universities shared with their colleagues in other university divisions the limitations imposed by the concept of university faculties as bastions of orthodoxy Just as Abraham Flexner found fault with medical faculties of his age and culture, so did Francis Bacon complain about the medical education of the renaissance, saying Medicine is a science which hath been more professed than laboured, and yet more laboured than advanced, the labour having been, in my judgment, rather in circle than in progression For I find much iteration, but small addition "[2]

Scientific Research in the Renaissance

Yet it is through medical faculties that universities received their initial experiences in scientific research One can see substantial beginnings of university scientific research in the work of Mondino and of Sylvius But the most significant example of early university research is that of Vesalius at Padua The publication in 1543 of Vesalius' great monograph, "De Corpore Humani Corporis Fabrica' marks a major contribution of the medical sciences to the scholarly strength of universities It symbolizes the concept that scientific research is a responsibility of university faculties This concept arose in faculties of medicine—more strictly, I am proud to say, in departments of anatomy These developments represented not only the beginnings of university scientific research, they represented the beginnings of modern biological research—neglected almost entirely since the days of Galen, thirteen centuries before

The contributions of Vesalius and other early renaissance anatomists had significance far beyond their impact on biology and on university practices and responsibilities They were of major importance in contributing to the shift from medieval to modern philosophy and outlook Vesalius showed that if one opened and examined the human body, one could see that the actual bodily structure was, in many ways, different from that described by ancient authorities In other words, direct study of a phenomenon is a more reliable guide to the nature of that phenomenon than is the word of some ancient sage or philosopher, however wise he may have been During the same age, great voyages of discovery had shown that if one actually examined certain portions of the earth, they were in many respects very different from the descriptions of Ptolemy and other ancient authorities Moreover, Copernicus, in the year 1543, the same year in which Vesalius published his treatise, came out with his revolutionary book on the motions of the heavenly bodies, showing that these motions could be explained and understood on a basis very different from that espoused by the authorities recognized at the time Thus university medical sciences share with the voyages of discovery and the writings of a Polish canon the presentation of convincing demonstrations that revered authorities may be unreliable, that knowledge of nature and of man depends on study of nature and study of man As Bacon put it, "Studies themselves do give forth directions too much at large, except they be bounded in by experience" [1] Medical scientists can look with pride at the contribution of their forerunners to the substantiation of these eloquent and true words

In the two centuries following Vesalius, the medical sciences continued to supply powerful impetus to scientific research within the university framework Here one finds anatomists continuing the illustrious role played by Vesalius Malpighi, Professor of Anatomy at the University of Bologna, in the second half of the seventeenth century, revived the science of embryology, dormant since the days of Aristotle twenty centuries before He introduced microscopic anatomy as a university research discipline and laid the foundations of plant anatomy and modern structural botany He was a leading practitioner of his day and a practical man of affairs

Reform of Universities

Happily, the concepts of scientific research found some footholds in universities outside the medical faculties Galileo and Newton were distinguished followers of the path pioneered by Vesalius But, in general, university scientific research was sporadic and unsustained in the three centuries following Vesalius It was best developed on the continent, but, with the single exception of Newton, found small place in English universities until the University of London was founded and Oxford and Cambridge were reformed as a result of external pressures in the mid-nineteenth century

The first sustained, continuous policy of fostering scientific research in universities on a national scale appeared in Germany following the Napoleonic wars At that time England was preeminent industrially and commercially Ingenious and practical Britons—and here, lest someone be offended, please be assured that I include the Scots—had learned to harness the power of steam, to use coal as a source of power on a big scale, and to contrive efficient machines for spinning and weaving The Germans realized that the commanding industrial and commercial lead of Great Britain could be overcome only by raising greatly the competence of the German populace They realized that knowledge is power They proceeded to organize their schools and universities to provide and disseminate the power of knowledge throughout the realm

In this magnificent flowering of German universities—which, in their maturity, became models for much that Flexner recommended for our own institutions—the medical sciences played a proud and effective part By way of illustration I shall cite the case of Johannes Muller of the University of Berlin This vigorous educator served much of his active life as Professor of Anatomy, Physiology and Pathology during formative years of his university which included the second quarter of the nineteenth century He came to wield enormous influence, serving eventually as dean of the Faculty of Medicine and as Rector of the University of Berlin From his vantage point in the medical sciences, he helped shape policies in education, in appointment and in research, which did much to bring his and other German universities to the lofty achievements which won the admiration of Abraham Flexner He was himself an enthusiastic investigator He saw clearly that it was his responsibility and that of all universities to train the men his society needed This he did with phenomenal success His vivid and inspiring teaching recruited able minds from his classes and from other universities into his research laboratory There he fostered and nourished a most amazing series of pupils Amongst them were Schwann, the father of the cell theory, Helmholz the man who gave us physiological optics and much of thermodynamics, Virchow, the founder of his famous *Archiv* and of modern pathology, Kolliker the author of the first textbook of microscopic anatomy, DuBois-Reymond, a pioneer in physiology, Henle, who described the loop in the nephron and who first required medical students to study anatomy with a microscope Muller demonstrated and established philosophies of teaching, of training scientists, and of practical academic administration which form the foundations of sound policies in universities today Flexner advocated for American universities and medical schools the policies which Muller fostered for the German

The Need for Education Today

I wish now to turn from reverence of past glories to contemplation of the present and sober consideration of the future What can and what should the medical sciences now do to contribute strength to universities? Before facing this question, let us ask, "How is the role of universities evolving in our society?"

With the great expansion of the population of this world and this country, with the accruing taxation of the irreplaceable resources of nature and of the world's available land, with the keen—if not bitter—indeed, sometimes vicious competition between nations for military, economic and political advantage, any nation needs vastly to increase its stores of knowledge, upon which success in every venture depends A nation must learn, or it will perish

If the government of a nation is to be likened to a person's brain stem and spinal cord, if a nation's transportation system resembles the cardiovascular system of a man, if our steel industry can be compared to the liver, then the universities serve a nation as the cerebral cortex serves a man *Universities are very important institutions indeed* If they are not properly nourished and supported, they will lack the strength to serve the nation as is needful A decorticate nation or an anencephalic nation will not last long in this competitive world

Those of us who are active today in the educational aspects of the medical sciences have sobering responsibilities indeed. I do not need to reiterate here that we must expand substantially the numbers of physicians we train and at the same time improve the quality of the individual medical school graduate. We all know that we must expand even more our production of medical scientists and teachers. But we cannot accomplish these aims if we focus our attention solely and narrowly upon medical education. For how can we improve substantially the quality of our graduates without improving first the quality of our faculties and the background and attitudes of the students admitted to our classes? Thus medical education is closely and inextricably tied in with problems facing our universities broadly. In order to attain the relatively narrow interests of medical education, we find it necessary to lend our support and energies to education in general. And this is even more imperative from the viewpoint of our duties to the nation and to humanity.

In common cause with colleagues in other disciplines who share the task of fortifying the bastions of learning upon which our nation depends, let us reduce our arguments to the basic essentials which can then be put in such dress as can be most effective and persuasive in enlisting public support. For today one can say as truly as did Francis Bacon three hundred and fifty years ago, that "states were too busy with their laws and too negligent in point of education."[4]

Today I think it is safe to say that many of our lawgivers and citizenry—yes, and even many of our corporation executives, excepting, of course, the well-known case of a General Motors executive—many of these people realize that our nation needs new knowledge and needs to disseminate more widely knowledge already at hand. We need knowledge of how to reduce the ravages of cancer and heart disease, knowledge of how to fire rockets straight and to fire them reliably, knowledge of how to get power from sea water, of methods for making profitable economic excursions into Asia or South America, knowledge of how to keep the Russians from getting control of middle eastern oil, of what to do about domestic farm surpluses or population surpluses abroad—and, no less important—we need a higher proportion of our people with the type of deep and sophisticated knowledge and understanding upon which national competence is based. Knowledge and understanding are the basic commodities with which a university deals, knowledge and understanding of man, the humanities, and knowledge and understanding of nature, the sciences. These are happily combined in medicine, the art of which, as Dana Atchley has aptly said, is "the skillful and creative application of a scientific discipline to a human problem."[5]

Thus universities deal primarily with knowledge. They are factories for creating knowledge. They serve as storehouses of knowledge and as centers for the metabolism and distribution of knowledge. Indeed, science can be regarded as the metabolism of ideas relating to nature. The knowledge dealt with in universities is made available to society principally through three channels. The first is through the medium of publication, whereby persons all over the world may be taught. The second channel is through the students who are taught and trained locally in the institution. Here, let it be emphasized the university's contribution is the knowledge and understanding in the graduate's mind, not the person himself. The third channel is through direct consultation and service rendered by learned members of universities.

Our society needs very much more knowledge if it is to survive. Most of this knowledge must come from and be distributed through our universities, including our medical schools. Thus these institutions must be substantially expanded and improved not just to accommodate and to benefit the students who will wish to attend in greatly increased numbers, but primarily and emphatically because the nation needs and will need even more desperately the knowledge which these persons will acquire and which will be processed in our halls of learning.

Financial Aid for Education

Thus expansion and improvement of our universities, including our facilities for medical education and research, is an urgent national need. This need is not currently being met. Far from it. All the resources of local tax support, of private philanthropy, of endowment,—all these must be mobilized and expanded to the fullest, but they cannot suffice. The need is far too great. The only agency which can provide the additional needed increments of support is the federal government. Federal support of higher education—whether it be through the front door, the back door or the chimney— is an urgent national necessity. Our universities are just as important national assets as are our armed forces—perhaps, in the balance, even more important. We benefit as a nation from the activities of universities. Then let us as a nation support our universities—support them adequately, through our national governmental machinery.

We have often been warned that we must not let federal support of education lead to political control. This warning is indeed well taken, but must not be permitted to impede the speedy mobilization of the substantial resources needed for the appropriate expansion and improvement of our universities.

It is in this area that the medical sciences can make a notable contribution to the scholarly strength of universities and to the national welfare. For the medical sciences in the United States have extensive experience with federal support without federal control. For about fifteen years the United States Public Health Service has provided support for research and for the training of research scientists in fields related to health. These funds have been administered through and by the advice of non-federal scientists of eminence and stature, whereby the public can be assured that the funds are expended on the basis of excellence and scientific merit, in the public interest, and without political interference This plan has important similarities to the functioning of the University Grants Committee of Great Britain, whereby substantial funds from the national exchequer are provided for the basic support of universities, entirely without political interference The great flowering of German universities was based on the liberal support of the Imperial German Government Our own armed forces are federally supported, yet our populace does not consider them to be under improper political influence

Thus the pattern set by the federal support for the medical sciences through the U S Public Health Service and the experience of the University Grants Committee of Great Britain provide the essential features, tested by experience, whereby universities can receive the federal support they urgently need without political interference

The development of substantial federal support of universities, including medical schools, though justified by urgent national necessity for the knowledge the universities provide and disseminate, will not absolve states, municipalities and philanthropists of their responsibilities to higher education Local support of medical schools and universities must be expanded because the localities need the benefits accruing from the presence of such institutions An outstanding university in a community provides a convenient local center to which its talented youth can go for individual betterment Such a university accumulates scholars of renown who contribute to the culture and wisdom of the community And, for the materialist who sets pre-eminent value on the dollar sign, an outstanding university, with its scholars, including scientists and engineers of eminence, with its computors, its laboratories, its particle accelerators, its institutes and its research contracts—such an institution becomes a magnet for industry, particularly industries based on intricate and advanced technology, through which local payrolls are supported and tax revenues accrue

There is a third party who benefits from the university This is the student Let us consider this matter in terms of medical education Since a student completing medical school and qualifying for practice finds his earning power enhanced, should he therefore assume a higher portion of the cost of his education and pay higher tuition fees? I believe not I believe the cost of tuition is already too high in our universities, particularly in our private universities, and that those who are able to present themselves for higher education are now selected too much on the basis of family means I believe it is sound to take the view that a qualified graduate of one of our medical schools is primarily an instrument whereby knowledge and skill relating to health and disease is made available to individuals in our society For embodying this knowledge and making it readily and effectively available, he is entitled to dignified material recompense But he should not be asked to pay personally in money for the knowledge he makes available for his patients It is sufficient that he apply the necessary time and diligence to his studies It is in the public interest to insure that opportunities for advanced study be made available to individual persons entirely on the basis of ability, merit, and diligence, without bias in favor of those with individual financial backing By this means, knowledge will become more freely available for the public benefit

Conclusion

In closing, we can look with pride at the past and with sober determination at the future of medical sciences as university disciplines We in the medical sciences claim honor that it was through our sciences that scientific research became a source of scholarly strength in universities We applaud the magnificent contributions to universities made by eminent medical scientists such as Vesalius, Malpighi, and Johannes Muller We share with our colleagues in other university disciplines the heroic challenge of bringing our universities, indeed, all our educational institutions, up to the level of effectiveness which our society will require Our product is knowledge and understanding, which our nation requires in far greater measure than it now receives This knowledge must be provided for society embodied in our publications, our graduates, and our services We must enlist the support, both federal and local, which will permit us to meet our country's needs We have shown a way in which federal support can be mobilized for scholarly purposes without political control We must see that the worthiest and ablest of our youth have opportunities to assume the task of making knowledge available to fellow citizens, without preference falling to youths from families of means

And so as we dedicate ourselves to this high calling, we take comfort in the realization that as we thus serve our country's welfare, we serve the welfare of all mankind

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THE UNIVERSITY—A SOURCE OF SCHOLARLY STRENGTH FOR THE MEDICAL SCHOOL

John S Millis, Ph D , Cleveland

The university is a scholarly resource for the medical school because of its particular nature and because it is organized for and operates to achieve certain specific goals Hence I shall attempt to express my beliefs on the subject of the university as a source of scholarly strength for the medical school by considering the nature of the university and by deriving from a definition of the university the specific scholarly contributions it makes

There are nearly as many definitions of a university as there are speakers who attempt to define it This fact is not due to any uncertainty about the matter but rather bears testimony to the great complexity of the entity which we call 'university" and to the fact that each one of us sees it from a specialized point of view which reflects our personal participation within the complex and dynamic institution Among the important aspects which must be included in a definition of a university are unity, pursuit of excellence, and concern for the future I shall organize my thoughts about the university as a source of scholarly strength for the medical school around these three aspects

Unity

The word university" literally means many or much in one We are accustomed to the many but frequently fail to remember the one Yet the true university must be and is a unifying force, for it cannot escape being concerned with the wholeness of knowledge Being concerned with wholeness, the university is a place where perspective is possible and present This aspect of the university is a source of scholarly strength for the medical school, for in the university there are scholars in all major fields of intellectual endeavor No learned profession can foretell in what directions its scholars are going to carry their investigations and therefore what heretofore unused intellectual resources they will require The installation of departments of biochemistry, physiology, pharmacology, and microbiology one-half century ago came about because of the need of the medical scholar for the knowledge and techniques of the chemical and biological sciences Currently we are seeing the rapidly developing use of the knowledge and techniques of other areas within the university Physical anthropology, biophysics, psychology, and mathematical statistics now appear in the instructional and research efforts of medical schools

A second resource which the university possesses because of its unity is the environment which it creates Any environment which is designed to encourage intellectual progress through scholarship must have both diversity and unity Without diversity, it will provide only limited horizons Without unity, it will provide neither standards, purpose, nor direction Freedom of inquiry is produced within this environment of both diversity and unity In a sense, freedom is the connecting thread of both diversity and unity This is probably the way in which the university best serves the medical school as a scholarly resource Without freedom and without an environment especially created for freedom no profession can long remain learned

The third resource which arises from unity within diversity is the direct effect on the scholar We all too frequently underestimate the effect of cross-fertilization and the stimulus of intellectual competition The awareness of the interests and the direction of the inquiry of one's colleagues on a university campus certainly has a profound and stimulating effect on the vitality and the boldness of every scholar The challenge of scholarly success in other fields is a direct stimulus to aspiration and to performance Scholarly competition is a valuable spur, for it prevents any single group of scholars from being too complacent about its own progress

The fourth resource arising from unity and diversity is the opportunity that the university presents for interprofessional cooperation The great problem of a free society in our complex age is the production of interpersonal and intergroup cooperation on a voluntary basis As knowledge increases in amount and in complexity, specialization becomes more intense and fewer and fewer services can be performed by a single person More and more services require the cooperation of several or many specialists The coordination of these specialized services by voluntary means becomes more and more important Only in a university, with its vast array of specialists, is it possible to provide the learning situations which foster the understanding and appreciation which must precede interprofessional cooperation

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President Western Reserve University

Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 8 1960

Pursuit of Excellence

If I had to give a single definition of the university, I would call it an institution created for the pursuit of excellence We usually call a university an institution of higher education, but we would be more accurate to call it an institution of the highest education The university carries the responsibility for instruction of the most difficult and most mature sort It awards the highest degrees and is entrusted with education for the learned professions A free society is one in which the individual person is permitted and urged to pursue personal excellence Thus the university becomes one of the prime means for accomplishing the central aim of its society Any university worthy of that name must aspire to and constantly pursue excellence

The pursuit of excellence provides scholarly resources to the medical school in four ways First, excellence is the constant goal before all its members Within such an environment the scholars, both junior and senior, find motivation, example, and challenge The pursuit of personal excellence becomes the mode of behavior for each of the members

Second, the professional faculties are constantly reminded that education for the learned professions requires not higher education but the highest education From this realization comes the setting of standards of excellence and the demand for scholarship

Third, the pursuit of excellence results in the elevation of standards Each faculty is encouraged to expect and to require more of its students Admission requirements are elevated and performance expectations are heightened Bright and strongly motivated students are a primary scholarly resource Further, standards of the freedom of inquiry are also elevated In an institution dedicated to the pursuit of excellence intellectual freedom is encouraged and becomes characteristic of the environment I can mention no single scholarly resource of greater importance than intellectual freedom The true university produces such freedom because it is dedicated to excellence, and in a free society excellence and freedom are inseparable

Fourth, intellectual vitality is generated by the pursuit of excellence Some have used the analogy of a running stream and a stagnant pool "Learning in a situation without research is like drinking from a stagnant pool, while learning in a situation with research is like drinking from a running stream" The pursuit of excellence requires research to enlarge horizons and scholarship to achieve intellectual satisfaction Thus the pursuit of excellence is itself the running stream which is a source of scholarly vitality for student and teacher alike

Concern for the Future

The third idea in my definition of the university has been stated by President Wessell in referring to the statements of Dr Lester Evans The university is the one organized institution of our society specifically charged with a concern for the future The research in which university members engage directly determines the directions of technological advance, the evolution of cultural and moral standards, and the determination of the values and mores of the society of the future The students they educate become the professionals and the citizens of the future No university can fail to be concerned about the future This concern for the future is another source of scholarly strength

First, it places research, the lifeblood of scholarship, in perspective The realization of the impact of research on the future demands that universities be responsible for accuracy and integrity of investigation This concern necessitates research, but it also necessitates scholarly responsibility It makes research a means to an end rather than an end itself It makes research moral and meaningful rather than amoral

Second, concern for the future stimulates flexibility in the educational process It demands a never-ceasing scrutiny of the educational process It requires that the educational process of the present be adequate for the foreseeable practice of the profession of the future Thus education becomes more vital, more adaptable, and less rigid in the university than it tends to become in the isolated professional school Thus the vitality of scholarship is enhanced by the university and the future protected

Third, the concern for the future adds a further dimension to the intellectual freedom and the spirit of inquiry of the university and, therefore, of the medical school When the mind deals with the future, it is further freed of limitation and its freedom of inquiry is enhanced Since change is inherent in the future, experimentation has greater justification and is substantially easier to accomplish

Summary

The medical school is an institution devoted to the education of those who wish to enter a learned profession The university is a seat of learning and by definition must be a place of scholarly resources, tangible and intangible Few will deny that these scholarly resources exist Some will point out that they are only partially utilized The central task of all higher education, the challenge to all educators, both those of the medical school and those of the university, is to increase the utilization of those resources

MEDICINE AS A UNIVERSITY GRADUATE STUDY

Maurice B Visscher, Ph D , M D , Minneapolis

When one proposes to speak about "University Graduate Study" one has the obligation to define one's terms Probably no two experts in the field have precisely the same constellation of qualifications in mind when they use such terms The least I can do is to give my own definition, and I can hope that it will not deviate too far from a generally acceptable one To my way of thinking, graduate study has only one generally unique quality, namely, that it is aimed at preparation for creative scholarship rather than simply for vocational or professional application of knowledge In this statement I distinguish sharply between postgraduate study, which is usually aimed at increased proficiency in applying knowledge, and graduate study, which aims at increasing knowledge The aims rather than the methods represent the first difference, but the methods also become different when sound preparation for creative scholarship is projected and carried out In making these assertions, I am not prejudging the question as to whether graduate study may not be of advantage to the practitioner of a learned profession such as medicine I am only recognizing the reality that there may be programs of postgraduate study that do not prepare persons for creative work

Historical Background

Traditionally, medicine has been among the learned professions Even in ancient times, before there was any science of medicine, the practitioners of the healing arts were among the more learned men With the growth of the university system, medicine, as well as law and theology, has been a foundation of the academic enterprise There is no doubt that medicine provided the nurture for the growing sciences of chemistry, physics, and biology in the postrenaissance era of western civilization

In several countries today the place of medical faculties in university structures is extremely varied The continental European tradition of matriculation in medicine directly after graduation from the high school is followed not only in most of Europe but also in Latin America and much of Asia and Africa In the United States there has evolved the system familiar to us of several years of premedical college or university training followed by four years of study in a medical college The system in the United States has changed greatly in this respect during the last half century after the Flexner report, which exposed the shocking inadequacies of medical schools in the United States At the time of the Flexner study, medical education in the United States was generally begun immediately after graduation from a high school and was usually of trade school quality One could not, at that time, have spoken of medicine as a serious university discipline except in a bare handful of institutions, perhaps fully only in one

Current Situation in the United States

Today in the United States, medical education is undoubtedly at a level enormously improved over that of the pre-Flexner days How much of it is really at a university graduate level is the question now One must examine the extent to which medical faculties in America have made medical education an opportunity for genuine study by developing scholars rather than having a series of drill sessions for hopeful artisans

A difficulty which arises immediately in considering these problems in the context of American culture is the fact that, in the United States, there is no clear-cut distinction between the high school and the university as to the responsibilities for independence and self-reliance on the part of the student Spoon-feeding is carried from the high school through the college or university into medical schools, to a very large extent The very word university has a different connotation in the American than in the European vocabulary To the American, a university may be anything from a college with no scholarly character but with ambitions to be looked on as important, to a collection of colleges in which work of scholarly character is carried on

Among the 85 medical schools in the United States today, only 1 admits students with less than three years of premedical college or university education Thus, after the first year of medicine, students are virtually all eligible for graduate school enrollment This, however, does not automatically indicate that the last three years of medicine are in general of graduate university quality, even by American standards No education is of graduate school quality unless it can or does lead to independent scholarship

I believe that the requirement that original investigation be carried out is not a superficial criterion of graduate quality of work Various medical schools differ greatly in the number of their medical graduates who have met this criterion of graduate school quality work in the degree to which they encourage and inculcate independent scholarship in their students In too many institutions the temporary mastery of a body of knowledge is equated with education This body of knowledge may be presented in segments corresponding to the various conventional disciplines or it may be

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premasticated and predigested into a so-called integrated curriculum, but in any case, as long as it is taught, rather than offered, as a part of a program of learning leading to creative scholarship, it is not graduate level education However, many medical graduates do become productive investigators One can ask whether this is because of, or in spite of, the character of medical school training, but it is obvious that a sizable number of graduates from certain medical schools do devote their lifetimes to teaching and research

Dickinson[3] presented a monumental study of the career activities of graduates of medical schools in the United States during the 30 years from 1920 to 1950 It appears that 0 9% of medical graduates were in full-time academic medicine and that the range in percentage for various schools was from zero to 4 2% over the entire span There was some variability over a period of time, as might be expected For example, in my institution in the period 1945-1949 the percentage was 2 8, while in the period 1940-1944 it was 5 2 For Johns Hopkins the figures were 6 7% in 1925-1929 but 0 5% in 1945-1949 In general, the period 1945-1949 was a skimpy one for interest in academic medicine, the over-all average being 0 5% for that graduation period The average had been 1 4% in the preceding five years World War II had much to do with this difference, no doubt, but exactly how it influenced it is hard or impossible to say

If roughly 1% of medical graduates devote themselves full time to academic medicine and if, as one can guess, that another 2 or 3% devote a significant amount of time to creative scientific work, one sees that the number of doctors whose careers are concerned mainly with advancing knowledge in medicine is still small Two points must be raised in this connection (1) this number, however small, is the seed for future crops and must have attention out of all proportion to its size, and (2) even for the person who does not enter medical research and teaching as a career the approach to professional medicine as an applied science may require that he have an opportunity to participate to some extent, even if only for a brief period, in the exploratory enterprise He may never be able to apply the science well unless he has at least been a part of a research team for a time

It is of interest to note what degree programs persons who now hold full-time posts in medical schools in the United States participated in during their years as students According to the Nov 14, 1959, report on medical education in The Journal, 81 6% of all full-time faculty in clinical departments, including pathology, in the 85 medical schools in the United States hold only the M D degree Of the remainder, 9 3% hold only the Ph D degree, 3 3% hold both doctoral degrees, and the residue holds some other degree Although it is obvious that, as far as formal degree programs are concerned, most clinical teachers and investigators have been limited to the medical training program, one should point out that many, perhaps most, of this group have had the benefit of much postgraduate medical study under another name In fact, there are probably few among them who have not had extensive training in basic science laboratories after medical graduation

As to full-time appointees in medical school basic science departments, the picture is different Except for pathologists, less than 20% of basic science faculties hold only the M D degree, 7% have both the Ph D and M D, and the remainder is made up largely of persons with Ph D degrees Thus, it is obvious that in the preclinical sciences the training of teachers and investigators has been largely the responsibility of graduate rather than medical schools The growing emphasis on more fundamental physics and chemistry in the investigation of the biology of disease, not to speak of dynamic biology generally, makes it likely that more rather than less emphasis will be placed in the future on graduate, as contrasted with professional, training for medical investigators

Combined M D -Ph D Training Program

In the institution with which I am associated there has been for about 40 years an optional honors course program for combined study for the M D and the Ph D degrees, the latter with a major in some basic medical science Special arrangements are made to provide flexibility in satisfying the requirements in various departments by such selected students Throughout this time, part-time assistantship subsidy has been available to assist such students In these 40 years, about a score of persons have earned both degrees, choosing physiology as the basic science field Recently, an experimental training grant of the United States Public Health Service has been set up to encourage greater utilization of this program, providing more ample subsidy for students engaged in this program To our chagrin, in the three years that this new program of subsidy has been in operation, only one adequately qualified student has applied for acceptance in this program with physiology as his basic science The other disciplines in the basic science area, such as physiological chemistry, anatomy, pharmacology, and bacteriology, have also had difficulties in attracting many highly qualified students into this program

The aim of the combined M D -Ph D program is to encourage students to become thoroughly grounded in a basic medical science to fit themselves for teaching and research careers either in clinical or preclinical medical fields The assumptions are made that preclinical scientists will be able to work more effectively after having full medical training and that clinical scientists need the deeper, basic scientific background Both assumptions seem almost indisputable Yet, for some reason, most students are either unconvinced or uninterested Further assumptions are that students contemplating careers in clinical investigation and teaching will see enough merit in three years of academic work in a basic science discipline to warrant the time expenditure and that those contemplating careers in preclinical science will think that a medical degree program will be more valuable to them than an equivalent effort in mathematics, physics, and chemistry might be. As to the value of basic science to a clinical investigator, it is hard to see any question whatever. As to the relative utility of time in the clinical medical fields and equal time in the sciences basic to the preclinical sciences, there is reason to think that it would be more valuable to learn about medicine than more about the bases of science only for the person whose interest in research lay in problems closely related to medicine.

Consequently, it may be that, for the future, the education of more basic medical scientists will be less a problem for medical schools and more one for graduate schools. This need not lead to a serious lack of medical orientation if the graduate departments are parts of medical schools. Students will still have much opportunity and incentive to orient themselves in the problems of the biology of disease.

Postgraduate Medical Education

According to the annual report by the Council on Medical Education of the A. M. A., there were only six institutions in the United States in 1959 which offered programs of study leading to the Ph.D. degree in clinical medical fields. Thirty-one offered work leading to M.S. degrees. By contrast, hundreds of hospitals and other institutions offer post-M.D. opportunities for advanced professional and scientific training not leading to any advanced degree. Formal graduate school programs with major emphasis on the clinical sciences are believed by many leaders in American medical education to be either useless, improper, or both. Some medical educators insist that an M.D. degree is a graduate degree and that another doctorate degree is meaningless and useless. Others suggest that the clinical fields are not sciences and that to treat them as such is a perversion and, therefore, improper.

As to the first supposition, namely, that present day medical school curricula in the United States are now of graduate character, the evidence is overwhelmingly in the negative. Unfortunately, there are only a few institutions in which the lockstep program can be broken by a student in the clinical years. The future may see some improvement. In my own institution, for example, there will be a certain liberalization next year by the provision of completely free elective periods and by allowing greater freedom as to time for completion of the several clerkship requirements. However, I shall be surprised if in the United States the time will come when, as in Europe, a medical student can spend the greater part of his entire course time (up to 80%) in a single discipline. In such a situation, one can acquire knowledge and develop research skills. The European M.D. degree can be a graduate degree. The medical degree in the United States cannot be a graduate degree for the person who spends the normal amount of time attaining it. Therefore, to say that further training beyond the M.D. degree is unnecessary would be nonsense. The question of whether a Ph.D. degree should be obtained in the postgraduate medical training program is another matter and will be considered later.

As to whether a graduate education program in clinical sciences is proper in the sense that a clinical field can be looked on as a branch of real science, I believe that history is answering this question. I take a dim view of graduate degrees with majors in the numerous smaller subdivisions of clinical medicine. To reduce it to the absurd, I doubt that proctology constitutes an organized field of knowledge large enough and rich enough in content to permit one to call it a major field in a graduate school. But fields such as internal medicine, surgery, clinical neurology, pediatrics, and ophthalmology are ones in which the present-day store of scientific knowledge is so great and the potentialities for the future so large that one can certainly accept them as respectable fields of intellectual activity. If such fields are inappropriate for graduate study, so are all fields in engineering and other applied sciences.

In other words, I reject completely both notions: the one that an M.D. is already a graduate degree in the United States, and the other that the major branches of clinical medicine are not suitable fields for major graduate study. Nevertheless, there is experience and evidence that the growing points of clinical medicine are situated in the realm of the more basic sciences. The University of Minnesota partially solves this problem by requiring that any candidate for a graduate degree with a major in a clinical field must choose a basic science for his minor field. Perhaps it would be better if the formal emphasis were reversed, but actually the candidate himself frequently, if not usually, reverses it in his program of work.

For the person who already has a degree in medicine, graduate study toward a higher degree has certain advantages. It compels more emphasis to be placed on basic science than might otherwise be given, it requires some foreign language proficiency, and it requires for its successful completion a demonstration of ability to search for and find some new knowledge. Of course, not every postgraduate medical student succeeds. In Minneapolis, our experience over the last quarter century is that about one-fifth of those who begin such programs in clinical fields actually end up earning a graduate degree. This is not a negligible number, however, an average of about 20 students per year are awarded such a degree. In the University of Minnesota, including the Mayo Foundation, about 1,000 students are registered for graduate study in the medical sciences About one-half are in Minneapolis, one-half in Rochester In Minneapolis, the number of graduate students equals the number of undergraduate medical students

It will be obvious from the fact that four-fifths of our graduate students do not earn higher degrees that we do not attempt to exclude from such registration persons whose primary interest lies in advanced professional training rather than in teaching and research in medicine For this the university offers no apology These persons obtain an experience in contact with the advancing front of medical science which can scarcely fail to improve their competence as physicians Furthermore, and this is perhaps the critical point, a large number of young doctors have been given an opportunity to taste the possibilities of a research-teaching career and the faculty has had an opportunity to select the most apt from a larger group to the end that, without much doubt, a larger number have entered research-teaching careers than would otherwise have been possible

As noted previously, less than 1% of medical graduates enter the field of academic medicine It is important that, by self-selection and external selection, this small number be the best of the talent in each generation, if not, the whole enterprise of scientific medicine will bog itself down with incompetence I do not know precisely how it will come about, but I predict that within a generation, all clinical investigators in the United States will have, in addition to the M D degree, either a Ph D or its equivalent in scientific training I do not foresee the professional medical training in the United States being lengthened or changed in such a way as to make it truly graduate education Therefore, to meet self-evident needs, it will be necessary to provide the training in science equal to the tasks of medical science in the future in other ways The Ph D program is one of the possible ways, and it may well be the best

Environment For Graduate Education

In his 1958-1959 Report of the Markle Foundation, John M Russell has made the following statement "Medicine is an art, a science and a business It is this last fact that causes the most trouble in medical education and, if allowed full sway, can ruin a medical school Members of the faculties can get so involved with the demands of patients and the attractions of a lucrative practice that there is no time left for students, not to mention research

"What can be seen inside some medical schools and in some clinical departments is not pretty While everyone understands the purposes of a medical school, strong leadership in carrying them out is too often lacking Too often the strongest personalities are in the clinical departments, not in the school's administration These strong men often have worldwide reputations in their clinical specialties, but are not necessarily the best informed as medical educators Being human, their vested interests tend to cloud their better judgment The problem is a mean one and must be solved by the medical educators themselves"

If devotion to scholarship in teaching and research on the part of faculties is an indispensable climatic factor in graduate education, and I am certain that it is, and if Russell is right, and I think he is, then certain social factors may be a major hindrance today to effective graduate education in medicine Atmosphere is something that can be spoiled by a small amount of bad odor Unfortunately, a very small percentage of money-minded persons on a medical faculty can ruin the atmosphere of an entire establishment When these persons are highly competent and highly respected by the public at large, it is small wonder that young men may see in them, if not models to emulate, at least excuses for their failures to pick better ideals

The problem is, of course, not entirely intramural as far as medical schools are concerned Society places so much more value on monetary success than it does on intellectual achievement that the marvel is not that so few choose to achieve the latter but that so many do It should encourage one about the basic integrity of the human animal that there are so many persons for whom the lure of flesh pots, Cadillacs, mink coats, and other popular symbols of status are ineffective Nevertheless, there is a very serious situation which, as Russell says, "must be solved by medical educators themselves" There are two obviously general solutions (1) for academic persons to resist the temptation to fritter their lives away for monetary gains, and (2) for academic institutions to set up such regulations which will make improper behavior impossible Human nature being what it is, the first probably will not work The second may be painful, but it seems necessary if medical schools are to maintain an atmosphere in which scholars are to be nurtured

There is another type of environmental influence which is perhaps most important of all the enthusiasm for knowledge The late Professor Starling said, "Research is a game" He meant that if one did not get pleasure out of the work itself, it was futile to try to be a scientist Henry Steele Commager speaking at a celebration for Dean Theodore Blegen, remarked, "There is nothing about the problem of recruitment of competent young scholars that enthusiasm for discovery and a little money won't solve" He had been discoursing on the importance of emphasizing the pleasures of the work of the mind to the upcoming generation As teachers, we are apt to reinforce the stereotype of the life of the scholar as a dull grind in our day-to-day assignment of tasks to our students Only by leading students through the story of the actualities of the road to discovery can they grasp the significance of the excitement side of scholarship Obviously, one does not have time, in learning about a subject, to follow all the ramifications of the trails that led to success in solving problems, but one can sample the terrain

The main danger in the growth of practical importance of science, including medical science, is the tendency to lose sight of the sense of adventure in the enterprise It is too likely to become a utilitarian enterprise in which only the practical results become important They are important, but it may easily be impossible to achieve them unless the student can enjoy the quest for knowledge as pleasure in itself

Finally, as Commager says, "a little money" is a necessary ingredient The amount depends upon circumstances It has to be enough to allow young men to justify themselves in the eyes of their wives and families for choosing the "game" of medical science for their careers, but not so much that they find themselves caught up in the distractions of the more commercialized world Some upper middle ground between poverty and affluence is probably the ideal economic position for the creative scholar, in medicine as elsewhere Society has not yet accepted responsibility for providing these upper middle class incomes, but it will need to do so if we are to have a proper climate for true university level graduate education in medicine

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MEDICINE'S DEBT TO ABRAHAM FLEXNER

Louis M Orr, M D , Orlando, Fla

Last September, an editorial in the "Chicago Tribune" contained the following statement "Abraham Flexner was one of the movers and shakers of his era The world is a different and a better one, thanks to his influence" The New York Times editorial said that 'No other American of his time has contributed more to the welfare of his country and of humanity in general" Dr Flexner made it possible for physicians to see clearly the direction of their efforts in medical education The size of medicine s debt to him can be appreciated by going back to the year 1908, when there were three classes of medical schools good, bad, and indifferent

Medical Schools Before the Flexner Report

Here is a brief picture of medical education in St Paul, Minn , around the turn of the century Dr A J Stewart wrote the following "The students, reading in the different doctors' offices, met in the second story of the little dead-house which stood to the left of the original building of St Joseph s Hospital The dead-house contained a table, chairs, and the inevitable skeleton Dissections were made there of amputated limbs, et cetera, from the hospital Regular instruction was given by members of the hospital staff"

It is occasionally forgotten that medical education in the United States has earned the right to be considered a professional discipline only within comparatively recent years As late as the first decade of the present century, the majority of American medical schools had staffs that were inadequate both in number and quality They possessed only meager physical facilities and conformed to practically no standards

Of the 150 medical schools which were in operation in 1905, only a handful offered an education program that could be considered adequate in terms of the type of training now generally provided Of the remainder, many were proprietary institutions operated for profit by their promoters or faculties Others were outright diploma mills Standards for admission were practically nonexistent Even a high-school education was often not required Some of the schools had nominal connections with universities, but in general they were organized to make money for the faculty Courses at most of these lecture mills were limited to two sessions of three or four months each There was no division into grades, and the pupils sat through the same curriculum twice on the theory that what they missed the first time they might understand the second Hospital and laboratory work was almost unknown

The proprietary medical school was a combination of lectures, quizzes, and cramming Its growth, like the growth of any other field in which the need is much greater than the supply, was from necessity and from greed Any physician could set himself up as a preceptor to train medical practitioners Practically any group of physicians could start a medical school, and many did

Unquestionably, many of those preceptors and physicians sincerely and conscientiously tried to meet the need for good medical instruction One doctor, who dismissed four students who had been studying with him for several years, was very frank to admit that, although he had made his books available for their study and had tried to teach them all he could about the practice of medicine, there were

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President American Medical Association
Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 8 1960

two things that troubled him "I am sure half of what I taught you is wrong This troubles me But the other thing which troubles me more is I am not sure which half it was"

Unfortunately, neither all preceptors nor all physicians who organized medical schools were motivated by such altruism Some saw the obvious advantage of having the services for several years of devoted, unpaid, and willing assistants Some liked the prestige of being known as a professor of a medical school Others profited substantially from the fees paid by the students

One can guess that the country contained many inadequate, obscure diploma mills Before 1910, Chicago alone had 15 As a result, there was no dependable way of knowing whether or not a diploma was genuine, forged, or stolen One kindly critic apologized for the proprietary type of school in the following way "One can decry the system—the inadequate preliminary requirements, the short courses, the faculty arrangement of the curriculum, the dominance of the didactic lecture, the meager appliances for demonstration and practical instruction—but the results were sometimes better than the system' Indeed, eminent men developed to enhance the profession, perhaps despite the system rather than because of it

The power of the private medical schools and the diploma mills was so great that the medical organizations of the country could only debate about the evil No real action could be carried through The matter of securing needed legislation in the various states to raise the requirements for licentiates was smothered by the practices of the politicians

Flexner's Findings

This, then, was the situation which is the basis for the debt to Abraham Flexner, a man who never rested with criticism alone Inevitably, where he destroyed, he led the effort to rebuild In his report, he stated that the nation's medical schools were "essentially money-making in spirit and object" and were multiplying without restraint, conferring a degree on any man "who had settled his tuition," whether he had regularly attended lectures or not He condemned American universities for offering "bargain-counter and chain-store plan education," for harboring "educational quacks," and for irresponsibility in turning out large numbers of poorly trained physicians who were overcrowding the medical profession

Appended to the report was a bulletin on each school, marked by such words as "disgraceful" and "shameful' One institution was dismissed as a "fiction" Chicago, with its 15 schools, was characterized as "the plague spot of the country" The state of Illinois had one official who was a valiant fighter for reform This was Dr John Rauch, head of the Illinois State Board of Health, which had charge of the examination of candidates for license to practice He carried on constant warfare against the low-grade and "diploma mill" schools So fierce were his attacks that the politicians marked him as an enemy He was removed from office in 1891, which allowed the state of Illinois to be overrun by the quacks to a degree worse than before

Although he was no muckraker, Dr Flexner highlighted abuses of the diploma-mill era with a skill that an Upton Sinclair might have envied He had no staff, and his final report was largely an account of what he had seen during his travels to more than 150 medical schools in the United States and Canada The report itself was a modest-sized volume written in precise language and contained a minimum of cross tabulations, footnotes, and academic jargon It went right to the heart of the problem Its contents were so damning that within months of its release nearly one-half of the schools had to shut down, and medical education benefactors learned to become extremely cautious in their contributions Dr Flexner has been described as a visionary who could raise money for visions and administer them when they became a reality He was instrumental in influencing philanthropic foundations to endow more than one-half billion dollars to American medical education and in opening doors to research and experiment

Abraham Flexner told a story which typified the attitude of many young American medical students in the years before 1900 The story recounts the time when Friedrich Muller, at the height of his career as a leading physician and teacher in Europe, was approached by a young American bearing a letter from a colleague in New York Muller asked the young man what he was interested in

"Oh," the young man replied, "in the subjects being investigated here, in the procedure followed in teaching, in the kind of patients you handle, in the organization of the clinic "

Muller, wincing a bit, offered to introduce the American to his chief assistant "You can go to him at any time, and you are also equally free to come to me whenever you please How long do you expect to stay in Munich?"

"I expect to be here all day," the young man replied

Memorial Resolution to Flexner

Unlike this student, Dr Flexner expected neither to learn everything in a day nor to bring about overnight changes in the profession He knew that progress in medicine takes time In a lifespan approaching 10 decades, he furnished ample proof that it does occur when it is sparked into being The death of Abraham Flexner on Sept 21, 1959, made it impossible to carry out a formal ceremony planned by the American Medical Association in his honor As a substitute, which contains all the gratitude of a ceremony, the following memorial resolution to honor the late Abraham Flexner was approved by the A M A Board of Trustees at its meeting in Dallas, Nov 29, 1959

At the request of organized medicine in 1908 and with its cooperation, the Carnegie Foundation for the Advancement of Teaching conducted an independent investigation of the nation's medical schools Abraham Flexner, a biologist rather than a physician accepted the assignment His tireless and courageous efforts involved a visit to each of the 150 so called medical schools then in operation His findings were published in 1910, a half-century ago this year

His report threw the spotlight of public opinion on the grave deficiencies in the majority of the schools The worst ones closed as a result Improvements were made in the remaining ones

The investigation and Flexner report accomplished in a few years what otherwise might have taken a quarter of a century, for the improvement of medical education and hence of medical care of the public It marked one of the most significant contributions and greatest advances ever made in medical education in the United States

The advocacy by Abraham Flexner of lasting ideals of free scholarship in a university environment as best for medical education, and his insistence on the practice of the scientific method by students provided valuable guidance that was an appropriate counterpart to his incisive criticisms His membership on the General Education Board of the Rockefeller Foundation from 1917 to 1929 did much to secure millions of dollars from philanthropists for medical education to implement these ideals

Therefore, be it resolved that the American Medical Association Board of Trustees pays tribute to the late Dr Abraham Flexner, who has left an indelible imprint of positive significance on medicine as a result of his educational ideals, leadership, critical inquiry, courageous action, philanthropic persuasion, and tireless efforts The whole community of medicine feels a deep sense of loss in the death of Abraham Flexner

Conclusion

A debt of this far-reaching kind can only be repaid by our continuing in his image and by always striving toward progress in the direction he has set for us Discoveries and advances in medical knowledge benefit society only if there are available well-trained physicians capable of supplying such discoveries with intelligence During the last 50 years, the health record of the American people has improved at a rate that has not been approached by any other large nation in history This achievement and the many other unprecedented health improvements are in a large measure the direct result of the advances in medical education that have been made during the same period

This great progress has been due largely to the freedom and independence which has allowed the schools to develop their own programs, neither haphazardly nor in complete self-interest The schools have accomplished this progress within the vision and knowledge of a truly professional framework set up by such men as Abraham Flexner, who defined a university as a place where scholars and scientists should dedicate themselves to four major tasks the conservation of knowledge and ideas, the interpretation of knowledge and ideas, the search for truth, and the training of students who will practice and carry on The preservation of this freedom and independence under which physicians can continue to follow both the leaders of their profession and their consciences is the best assurance that medical progress in the United States will reach even greater heights of service to humanity Such preservation is the only real payment that can be made on the debt to Abraham Flexner

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COMPETITION FOR HIGH TALENT

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The concern relating to the subject of competition for high talent is one which is becoming increasingly manifest in a great variety of subject fields, among many professional organizations, and among many lay groups The competition to recruit talented youths by the many specialized segments of our fields and professions seems certain to become an ever increasing concern of each activity segment of our intricate technological and industrial society

It was this concern which led to the existence of the office where I serve The practical cessation of graduate training during World War II, the advanced level of activity in the sciences, and the extraordinary stimulation of technology and science in and after the war produced an apparent disparity between the requirements for personnel of advanced training and the oncoming supply Positive steps seemed indicated to call attention to facts and point to needed action

Agencies for Recruitment

Since that time, additional agencies primarily created to deal with the situation in their own fields have been organized The Engineers Joint Council, representing the several major engineering societies, has established an engineering manpower commission, which concerns itself with the training, utilization, and recruitment of personnel for that field A similar scientific manpower commission is active along the same lines for the scientific societies These two agencies are becoming increasingly aware that their functions are continuing and

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Director Office of Scientific Personnel National Academy of Sciences National Research Council

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that one can not foresee, at this time, any comfortable plateau when their services will no longer be essential.

The federal government has taken steps which indicate an acceptance of the premise that recruitment and the subsidy of training are necessary and are matters of national concern. The National Science Foundation maintains a substantial committee aimed at gathering facts on manpower supply and requirements against which national programs may be calibrated. The foundation sponsors large fellowship programs in the sciences. Under these programs some 2,500 candidates for the doctoral degree in the several sciences, including engineering, are supported each year. The foundation assists in other ways, such as by supporting basic research and, as a by-product, supporting many persons in training, consequently, it is a factor in recruitment into the scientific professions. The National Institutes of Health administer similar programs, somewhat more directly oriented to fields basic to the medical sciences.

The provisions of the National Defense Education Act are largely of a recruitment nature aimed at recruiting for and strengthening the faculties of our educational institutions through fellowship programs and other recruitment devices. Recently colleges acting in groups have begun to seek independent support for the establishment of fellowship programs to recruit and train for college faculties in their own domain. Other examples that could be mentioned are the programs of the Social Science Research Council and the American Council of Learned Societies. A pattern of recruitment by the use of special fellowships and other devices is firmly rooted in our practices and traditions.

Recently, in a number of fields, there have been studies aimed at assessing the growing needs and opportunities in the field in which the personnel equation has come in for separate and close scrutiny. For example the recent report of the National Academy of Sciences on the field of oceanography indicates the great need for expansion of the scope of our national commitment in this field and emphasizes the need for recruitment, by formal organized programs. The same sort of concern has been expressed in the field of space-related sciences, meteorology, and other areas.

The matter has become of sufficient moment that the Bureau of Labor Statistics is steadily increasing its coverage of the specialized professions. The President's Science Advisory Committee is concerned with this matter. The Office of Civilian and Defense Mobilization has established a committee on specialized personnel through which advice and counsel may be transmitted to appropriate government agencies.

In a sense, the society in which we live is a peculiarly unresponsive organism in matters of this kind. Primarily the mechanism of recruitment is the system of schools and colleges which make up our educational structure. Ours is, however, a highly decentralized structure with local control by schools, colleges, and universities of their own educational programs. In the United States change takes place primarily as a result of widespread understanding of the needs of society and cumulative action. There is an inevitable lag between the changes and the needs in society and the responses of the recruiting mechanism. This is difficult at present because of the speed and the fundamental nature of the changes which are occurring in our society and its many specialized activities.

Scientific Revolution

The scientific revolution which has been occurring in our world in the present century has now flowered into a movement which is dominant in the progression of events. The nature of that movement and its effects are the dynamic forces with which we are dealing in this matter of burgeoning needs for persons of high talent in so many activities, old and new. For this reason it may be worth while to point to a few facts which can serve as a point of departure.

The rise of science in the world is essentially a recent phenomenon, as one views the long perspective of history. It is only about three centries, a mere 12 generations, since the basic framework of theoretical science was established in the age of Newton, Leibnitz, and Galileo. It is not much over a century ago that the applications of science to the creation of a technology industry took place to any substantial degree. Within the memory of living people the large part of all that is considered technology today has been created.

The major factor in this enormous thrust forward has been the development of organized research and development on a massive scale. Prior to the 20th century, research was largely a personal activity done mainly in universities. Today it has become a heavily subsidized, highly organized and systematized, and highly competitive activity. Fundamentally, it remains an activity which depends greatly on personal competent, but the pace and power of the effort are enormous.

It has been said that we live in an age of discontinuity. The speed of lomotion available to manned vehicles increased very slowly up to 1947 and then suddenly shot upward with the advent of jet propulsion. The increase in speeds from the days of horse-drawn conveyances to the days of World War II combat planes was only by a factor of about 10. The advent of jet propulsion has increased available speeds by hundreds, and theoretical limits to the speed of jet-propelled vehicles are in doubt.

The power of explosives increased slowly up to the time of the nuclear explosion at Alamogordo and then suddenly increased enormously. Prior to World War II one measured explosive power in terms of tons of TNT. Since the advent of atomic explosions one measures the power of an explosion in megatons. The power of research, because of its new emphasis and enormous subsidy since the war, has increased sharply and discontinuously in this same sense The motivation behind this great expansion is that research is now known to be profitable, and it is closely related to national prestige, welfare, and security

Changes in Economy and Personnel

The resulting implications for the competition for high talent are discernible They are obvious in the fields which are involved in rapid expansion The national funds for performance of research and development have increased even since 1953-1954 by a factor of well over 100%, and they are estimated by the National Science Foundation to reach 12 billion dollars in the fiscal year ending June 30, 1960 This is at least 50 times comparable expenditures in 1940

While national expenditures are embarked on a rising curve with a rate of change quite different from prewar years, the rates of change in the training of personnel have continued along historic trends with little change In the United States training to the doctorate level has increased steadily at a remarkable pace of about 7% per year This is continuing mainly in the fields of the biological sciences and the nonsciences In the physical sciences, where the sharpest demand occurs, there has been a leveling off, numbers have about remained constant for the past six years Research and development have increased sharply as a result of national effort, and they comprise one of our largest industries at the present time But advanced training in the sciences has followed traditional trends

In regard to competition for high talent, the direct effect of this movement is to create a requirement for personnel to carry on these functions and activities However, the less direct results are equally substantial

Some of the effects of the explosive force of the new technological and scientific knowledge are rapid changes in our standard of living, in the nature and problems of our industrial administration and ways of living, and in the nature and urgency of rapidly burgeoning problems of a social, political, or spiritual nature in the United States

The changing standards of living present problems in the maintenance and service functions This is manifest in the fact that, for the first time in the history of the United States, service functions enlist over one-half of the labor force, and not only in the functions of servicing and maintaining household gadgets The maintenance, service, and operation of complex military, industrial, and research equipment such as electronic computers, automation devices, and complex vehicles of all types has created a demand for technicians of a different order of ability and training

Management has become a highly technical discipline, calling for higher personal competence and potential for growth It calls for more people who have a higher technical competence and training This is a matter which is becoming an item of concern in the training of personnel as larger numbers of persons must be expected to move into administrative positions

Management consultant firms have stressed problems of recruitment to high managerial posts Many management positions now require persons with strong technical backgrounds, and these positions draw persons away from technical work It has been reported that one-third of the enrollees in the Harvard School of Business have engineering degrees

Problems of Social Nature

Problems of a social nature, resulting from the rapid changes in society, now require new techniques and insights and more well-trained personnel The problems in our economy will require new and more quantitative techniques for their solutions In communication, transportation, and other requirements of a complex society, the problems of adjustment to a rapidly evolving society are great and will requires more well-trained and qualified people

Two important factors in this matter require special mention One of these is the impending increase in the national population This is of particular importance to the healing arts and other professions where the numbers of personnel needed have some more direct relationship with the growth of the population

At present, however, the population in the so-called productive age group is relatively small In recent years the population over the age of 65 years has greatly increased as has the population of those under 15 years It is the age group between that has been markedly thin The age groups 15 to 19 years and 20 to 29 years make up the smallest percentage of the total population in the past 100 years It is from the age group now in this middle category that people must be recruited and trained for the many functions I have outlined in previous paragraphs

The probable boundaries of this population growth have been outlined in a recent publication of the Population Reference Bureau, based on an important volume, Changing Population of the United States," published by the Social Science Research Council According to this report and on the basis of present trends, it is predicted that the population of the United States will approximately double in the next 40 years and will reach 350 million people This amount is astonishing largely because the drop in the birth rate during the 1930s served to overemphasize the population trends This trend has now reversed itself A major factor in the population growth trend, however, is the increased life expectancy affecting particularly the young and the old The expectancy for children at birth has increased about 50% While these projections are based on assumptions of present trends, even assuming a return to the slow birth rates of the years immediately prior to World War II, population increase rates would be great in comparison with past experience due to a larger population base and greatly reduced mortality.

While these prognostications are subject to unforeseen developments, one can hardly count on such developments. The fact probably is that children now in school and in training for eventual professional service in the professional labor force will be living in a world with a population at home and abroad so much greater than is now the case that the nature of that society will of necessity be different in many ways now unpredictable.

It is worth emphasizing that these predictions are not something for future generations alone to worry about. These situations are indeed imminent. The children now in the elementary grades will be at the middle of their careers and will be the leaders on whom society will depend 40 years from now when the population of the United States will likely be 350 million. The largest factor in this enormous rise in population growth has been the notable success of the medical sciences.

The impact of such populations on the available medical care, technical services, rate of use of raw materials, food and fibre, transportation, communication, and especially the need for service personnel seems likely to concern in the future.

Problems of Education

Mention needs to be made of the future demand for teachers. This has been so publicized as to require little reiteration or emphasis. The facts have been noted repeatedly by federal and nonfederal agencies. By 1970, for example, we shall need 300,000 additional college teachers just to meet rising enrollments. These plus others to replace retiring teachers present a staggering demand for personnel for the purpose of education alone.

That the school population is increasing has been well publicized as has the fact that college enrollments have increased because of the increasing size of the age groups yearly and by the increasing percentages of the age groups going into and through college.

In the United States so much attention has been paid over the years to the problem of assuring that able youths have the opportunity to go on to advanced training that the percentage of the ablest youths who go on to college has apparently greatly increased. Perhaps this is a direct consequence of the stimulating effects of such programs as are now found in some states where systematic testing and counseling occur. Perhaps such agencies as the National Merit Scholarship Corporation have been highly successful in talent identification, stimulation, and support.

It is known that the percentage of high school graduates who go on to college is substantially higher the higher the scholastic aptitude as measured by current tests. At higher levels, among those who have an Army General Classification Test score of 131, as many as 85% of male high school graduates may enter college. Even of those with as low a score as 118, probably three-fourths go to college. For the age group as a whole about one third go on to college. This is, on the one hand, reassuring as the talent loss in the upper levels of ability may not be as great as some have supposed. On the other hand, it indicates the narrow margin of untapped resources that is available. Statistics indicate that the tendency of female high school graduates to go on to advanced training is much less and the tendency to enter the professions is still less. It may be that more women in the professions is imperative measures for the future.

The mere assurance that youths of appropriate talent enter college is not enough. In spite of the steady increase in college enrollments, we have seen that freshman enrollments in engineering have dropped for two successive years in number and considerably in the percentage of all enrollments at the college level. There have been some increases, notably in physics and mathematics, but the numbers here are small to begin with.

It seems likely that the eventual effort at recruitment, whether it be for the healing arts, the sciences, or the other activities in our society that require high competence and extended training, must begin in the lower levels of the educational system. There are some good secondary schools in the United States, but there are many where the tangible evidence of good work is not reassuring. There are high schools which send a high percentage of students on to higher education and others which do not. There are enormous differences among high schools in the numbers of graduates who go on to college and continue on to do advanced work for the doctoral degree. Some high schools have large numbers of graduates whose names appear on the roles of doctoral graduates every year. Most high schools have none. The same is true in the field of the healing arts.

Comment

The competition for high talent is entering a phase where each specialized field is concerning itself more and more with positive, competitive steps to assure an adequate inflow into its ranks. This is natural and not to be discouraged. But concerted efforts to increase the total pool from which all may draw is even more necessary. The total age group of oncoming youths is inflexible as none of us can change the trends in population growth. We must draw from the pool the youths who have been properly educated and trained, well motivated to begin serious work at the college level, and who possess the basic disciplines and skills to do successful work

This century has seen a logarithmic increase in the demand for specialists, whereas the population has increased slowly and linearly These curves are diverging To alleviate the divergence of supply and demand, greater success will be needed in identifying training and motivating more people in the areas where their endowments indicate they can serve successfully It will not be enough to bend our efforts toward recruitment at the later stages of education This is a problem for the educational system as a whole

We who are in the professional ranks today are the trustees of those professions and their accumulated heritage We have the responsibility of carrying on this heritage by assuring that we shall have an adequate body of successors to carry on the work of the professions Most of us have been content to meet this responsibility by worrying about our own immediate training problems It seems likely that in the future all the professions will need to realize that the beginning of professional training is at the time the child begins to go to school The problem of education is one integral problem and not one coming in temporal and unrelated segments A concerted effort to improve all levels of education can probably best serve the interests of each claimant group in the quest for high talent

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PROVIDING PHYSICIANS FOR THE UNITED STATES—THE QUANTITATIVE PROBLEM

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In December, 1958, the Surgeon General of the Public Health Service appointed a consultant group to study and report to him on the question of how the United States is to be supplied with an adequate number of well-qualified physicians This group was a distinguished one and was well qualified for its job Among its members were three medical school deans, five other college or university administrators, two regional education directors, six executives of professional associations, two representatives of business and industry, and three others whose interests and experience were in closely related fields Its chairman was Mr Frank Bane, former executive director of the Council of State Governments The report was submitted to the Surgeon General in September, 1959

The basic finding of the consultant group is that the United States faces a growing shortage of qualified physicians My objective is first to give some of the evidence on which this conclusion is based and then to describe briefly the group's recommendations as to how this shortage may be alleviated

Several phenomena have combined to create a growing need for physicians for the United States Basic among these factors is the growth of the population Over the past 10 years, the population of the United States has increased more rapidly than the supply of physicians, with the result that the ratio of physicians to population has slightly declined The outlook for the next decade is for a further decline in the ratio of physicians to population

But, it may be asked, is the number of physicians in relation to population really a sound index of the need for doctors? Other things being equal, more doctors are needed for more people But do not such other factors as the kinds of service required from doctors and the development of more efficient methods of treatment also determine how many physicians are enough? They do indeed Therefore, the consultant group examined next the trend in the use of medical services

Growing Demand for Services

The consultants found that the growth of the population has been proportionately greater among old people and children, who require the most medical service While the population as a whole is expected to increase about 30% between 1960 and 1975, the number of children under 15 years of age will increase 35% and that of people aged 65 and over will increase almost 40% in this 15-year period Requirements for medical service are particularly great among older people, who make more visits to the physician and spend more days per year in the hospital than the rest of the population If these needs remain constant, the population in 1975 will need more medical services simply to provide care for a larger proportion of people in the oldest and youngest age groups

We cannot expect a trend toward less use of medical services Medical progress, in providing

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dramatic new treatments and preventive measures for conditions that formerly resulted in death or lengthy illness, has also brought new functions and responsibilities to the physician Improved economic status and increasing educational achievement have tended to be accompanied by greater use of physicians' services Growing concentration of the population in cities and the extension of hospital and health insurance to an increasing proportion of the population are two other factors that promise to increase use of doctors

That there is a trend toward increased use of medical services by the people of the United States is not just a matter of conjecture There is evidence that today people are getting more medical care than ever before Thirty years ago, the average person saw a doctor two or three times a year, now the annual average is five visits These changes have occurred in all age groups The young, the middle-aged, and the old all have shared in receiving more medical service

Right now there are unmet needs for physicians services in the United States There is increasing public recognition of the continued failure to provide adequate medical care for the mentally ill, a recent study of the American Psychiatric Association showed that the public mental hospitals of the United States needed 3,700 physicians to meet the minimum standards of the Association Requirements for physicians for teaching, research, and public health also are great and can be expected to increase further

We have seen, then, that the population is increasing faster than the supply of physicians and, further, that present tendencies indicate that there will be an increasing demand for physicians' services To reach a sensible conclusion about future needs for doctors, it was necessary for the consultant group to look at the physicians What are the changes occurring in the characteristics and organization of physicians that may have a bearing on their ability to provide medical services?

Changes in Medical Practice

One important finding of the consultant group with respect to the physician population was that an increasing proportion of our doctors are now employed in hospital service, teaching, research, industry, administration, and other types of institutional practice These developments have made possible much of the progress in modern medicine They have also been associated with a complementary reduction in the proportion of physicians in private practice

To the layman who measures the supply of physicians mainly in terms of the number of private practitioners available to give him service, this growth of new types of practice means fewer doctors Although the total supply of physicians in relation to population is about the same today as it was 30 years ago, the ratio of physicians in private practice to population has dropped by about one-sixth If present trends continue, the ratio of physicians in private practice will drop further

An increasing number of private practitioners now limit themselves to specialty practice, which adds to the need for physicians Each group of specialists has an essential role in providing us with good medical care However, the number of doctors who can be called family physicians, including specialists in internal medicine and pediatrics as well as general practitioners and part-time specialists has declined not only in relation to population but also in absolute numbers, from 117,000 in 1931 to 102 000 in 1957

Another finding of the consultant group on the physician population was that the United States is relying increasingly on physicians educated in other countries Of the 7,800 physicians newly licensed to practice in this country in 1958 some 1,300, or about 17% of the total, were graduates of foreign schools Only about one-third of these foreign school graduates were United States citizens who had gone to other countries for their medical education The number of foreign school graduates admitted to practice each year has increased threefold since 1950

An even larger number of foreigners are serving as interns and residents in American hospitals In 1951, there were 2,100 aliens serving in this country as interns and residents, by 1959, the number had quadrupled, to about 8,400 As a result, about one-quarter of all our interns and residents now are foreigners In some geographical areas, the proportion is considerably greater

Possibilities for more efficient use of physicians' time appear to be limited in scope The average physician in private practice can hardly be expected to work longer hours in order to improve his efficiency, for he now works some 60 hours a week Most doctors already have cut to a minimum the time-consuming home visits and see most of their patients in their offices or at a hospital Even organized medical care plans that have good facilities and what is considered to be a proper balance of staff use as many doctors in relation to population as are used by the country at large

Minimum Goal

How many physicians will the United States need in the years immediately to come? To improve the supply of physicians in areas of the country now less well served, to provide necessary services to the young and the aging, to keep up with growing demands for private medical services, to meet requirements in mental hospitals and public health, to compensate for the decreasing share of physicians engaged in private practice, to increase the number of family physicians, and to reduce its reliance on foreign physicians the country shall surely need at least as many physicians in relation to population as it has today.

The consultant group's goal of maintaining the present physician-population ratio over the next 15 years is therefore conservative. A recent report of the Rockefeller Brothers Fund, "The Challenge to America: Its Economic and Social Aspects," sets a higher goal. That report states: "We are short of doctors in many parts of the country and also of many categories of medical specialists. The number of doctors should increase in relation to total population" (p 57).

In order for the minimum goal of maintaining the present rate of supply to be met, 11,000 physicians must be graduated annually from United States medical schools by 1975. This is an increase of 3,600, or about 50%, over the present number of graduates. Only about 500 of these additional graduates will be provided under expanding or planned programs. The remaining 3,100 must be provided by further expansion of existing schools, establishment of new programs of the basic medical sciences, and establishment of new four-year schools.

The consultant group found that the supply of able young persons entering the medical profession is not keeping up with the needs even of existing medical schools, which further complicates the problem of expanding the capacity for medical education. As the length and cost of a medical training have increased and as more attractive opportunities have developed in related fields of specialization, there is some evidence that the average quality of medical students has declined. Schools with rigid restrictions on the admission of out-of-state students have tended to have particular difficulty in maintaining a high level of student quality.

One of the obstacles to the choice of medicine as a career is the high cost of training. Contributing to the cost are high tuition fees, relative lack of scholarship aid, limited ability to work part time during the school year, and low pay for interns and residents. The length of the course, 5 to 10 years of graduate training, intensifies the problem. Another deterrent would seem to be lack of opportunities for medical education in the area where the students live. The consultant group cites the example of Florida as demonstrative of how establishment of a new school may increase the number of young people receiving a medical education. Between 1950, when the state had no medical schools, and 1957, when both the Miami and Gainesville schools were in operation, the number of Florida young people who were first-year medical students increased from 2 per 1,000 to slightly above the national average of 4 per 1,000.

Recommended Action

To meet the United States' need for qualified physicians, the consultant group recommends the expansion of existing medical schools and the development of some 20 to 24 new two-year and four-year medical schools. They urge additional low-cost loans and scholarships for young people who would otherwise be unable to finance a medical education. They warn against expanding the number of physicians trained without adequate safeguards to the quality of schools. Tapping of all available sources of funds will be essential to the support of necessary research, operations, and construction of facilities. Fundamental at all stages will be careful and imaginative planning for future programs and facilities.

No single group within our society can be expected to accomplish these objectives alone. Private citizens, foundations, industry, professional associations, medical schools, universities, and the various levels of government all have a role to play. It was agreed among the consultants that the federal government must assist in providing necessary financial aid to students and also in meeting the often prohibitive cost of constructing new medical school facilities. The role of state and local governments is seen as being particularly in the development of financial aid programs for students, in the financial support of medical school operations, and in planning for the expansion of medical education facilities.

It is the last of these points that I particularly want to emphasize because it is on the soundness of the planning for the expansion of medical school facilities that all else depends. The consultants urged that states without a planning group on higher education develop such a group, which would have planning for medical education as one of its functions. They also urged that states develop interstate cooperation so that need and sources of support can be studied on a regional basis. They stressed the importance of concentrating such facilities in areas of the country that have few physicians in relation to present or projected population and inadequate medical opportunity for their young people and at the same time are able to support medical schools.

On the basis of the interest that has been shown in the consultant group's report, I believe it is safe to predict that Congress will consider proposals for aid for expansion of medical school facilities. While I am not willing to predict what the decision will be, I will go this far: I do not believe there is any time to be lost in getting the planning underway. It will not be accomplished quickly or easily, and so much depends on it. It would be difficult to overrate the importance of such planning, the consequences of not making careful plans and of not meeting the growing demand for physician services would be severe. The pattern that is set in the near future, whether it is action or default, will be felt, inexorably, for a long time to come.

NEW FACES FOR A NEW ERA IN MEDICINE

Raymond G Bunge, M D., Iowa City

Physicians and patients of the United States are members of the American culture Together with their fellow citizens they live in a common physical environment and are immersed in a social milieu of conventional beliefs, customs, behavioral patterns, and activities It is difficult to escape the deluge of visual and verbal symbols of native culture unabashedly poured forth by word and picture machines, the controllers of which strive ceaselessly to satisfy a voracious public appetite of bulimic proportions Rapid, economical transportation systems foster easy access to far-away regions and locales, in the United States, people love to travel and like vacations, and their commercial enterprises often impel distant relocations of their homes Having no propensities for being hermits and rather given to making and hearing talk, they are, so to speak, over their heads in the lively American scene

Immersion in the social milieu begins in infancy, and one must struggle to but glimpse, objectively, the automacy of his beliefs, behavior, and patterns of thinking and to see how language and symbol manipulation may subtly guide one to unrealistic conclusions and decisions It has been only during the past one-half century that sufficient knowledge has been accumulated for man to be able to view objectively his social environment Much has been learned of the general nature of civilization—its origins, its chief avenues of transmission, its progress, and the nature and source of cultural changes It is with these changes that I am principally concerned, for their magnitude and intensity account for the immense and heterogeneous present-day medical problems

The Fermenting Cultural Milieu

Cultural changes result largely from advances in technology such as tool-making, better instruments and techniques, and diverse applications or acquisition of new knowledge Man is a restless, curiosity-possessed, inquisitive animal and, given new materials and opportunities, he invents, discovers, and acquires new information, the hard stuff of a culture

Such technological advances are not bound to any creed or cult but are determined and evaluated on the basis of the available evidence Facts govern, and there is an appeal to reason Dr William Beaumont[1] paid tribute to the sovereign nature of facts when he wrote the following "I submit a body of facts which cannot be invalidated My opinions may be doubted, denied, or approved, according as they conflict or agree with the opinions of each individual who may read them, but their worth will best be determined by the formulation on which they rest—the incontrovertible facts"

A forceful, rational, factual appeal is difficult to ignore and demands attention But do people exercise such scrutiny when examining the myth produced beliefs or the untidy value systems of their society, as crystallized in their political and social institutions? For example, one would not have difficulty in explaining the advantages of the automobile over the horse-drawn carriage to a reasonable person, but could such explanatory review and arguments be brought to bear on a strongly-held cultural concept that "Automobiles are the machines of the Devil, should be avoided, and, where possible, destroyed?" Such cultural attitudes do not have foundations upon reasonable tenets and are invulnerable to factual arguments However, if the use of automobiles solves practical cultural problems of transportation, presents opportunities for profit-making, and augments survival in war, then the sheer weight of reason may force a change in the tenaciously held cultural concept, modify it, or cause complete abandonment The flexibility exhibited by reason is not matched by an easy alteration in cultural behavioral patterns as manifested in institutions The former engenders and promotes change, the latter resists it Of such rigidity is derived the commonly recognized cultural lag

The tempo of change has quickened Before people can adequately adjust, from a conceptual standpoint, to one technological advance, another comes on the scene demanding just as urgently philosophical consideration These technological alterations demand corresponding cultural adjustments of beliefs and practices—adjustments which are many faceted, far-reaching, and profound Accordingly, the pressures on institutional concepts rise apace The cultural fermentation now bubbles vigorously to a level of urgency and survival The awkward moral flabbiness of the people of the United States in the prospects of extermination by nuclear weapons, their relative lack of interest in the disparity between the well-off and the poverty-stricken peoples, and their attempts to control world population by quotations and magical incantation instead of by rational practical means indicate a lag of dangerous proportions How quickly will people realize that they are interdependent? Is there not great need for them to examine the roots of their own inflexibilities, fatalistic predilections, and concepts of happiness? These questions are, in part, a measure of the mounting social pressure arising from the impact of technological innova

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Read before the 56th Annual Congress on Medical Education and Licensure, Chicago, Feb 8, 1960

tions upon cultural value systems When institutions, which are the keepers of such systems, are under prodigious fire, man struggles to identify himself He may well ask, 'Who am I?', 'What shall I believe now?', What is security?", and many other pertinent or impertinent questions As long as only unsatisfactory answers are forthcoming, social tension will rise One hears much talk about adjustment, failures to adjust, incompatible social personalities, tranquilizers, gastric distress, and hypertension, all of which are overt personal manifestations of sociopsychological conflict

What is the social character of men caught in this era of rapid change? Dr Allen Wheelis,[2] writing about the emergent social character, has this to say 'The social character now coming to prevail seems sculptured to fit a culture of change In order to survive, it would appear that the individual must become progressively more able to modify himself, to alter his values, to change his reactions The currently developing social character is equipped with precisely this potential In it the light touch supplants the firm grip, the launcher of trial balloons replaces the committed man One avoids final decisions, keeps everything subject to revision and stands ready to change course when the winds change The key words of our time are flexibility, adjustment and warmth as for our grandfathers they were work, thrift and will" (I interject that the observations of many teachers that today's students are apathetic, lack purpose, and are not filled with work, thrift, and will may well find their genesis in this observation)

Medicine, Institution, and Technology

It is in this cultural embroilment that medicine stands today, subjected to all of the technological changes and the subsequent social pressures on its value concepts such as physician-patient relationships, choice of physician, payment of fees and medical service Physicians in the United States have cherished the concept of service, for example, repeated in a recent report of a committee of the American Medical Association[3] Medical care is that service which uses every means to secure and maintain a state of physical and mental well-being in the individual Good quality medical care results from the full use by the physician of his art, skill, and knowledge, and his utilization of scientific facilities available to him It depends upon the physician's sincere interest in the patient and the patient's faith in him'

How many patients receive this type of care? How many can afford it? Is the concept of private practice keeping pace with the rightful medical needs of society? To whom does the medical knowledge that physicians possess really belong? Such questions exemplify the mounting pressures on the institutional verities and on the eternal truths of the medical subculture

Technologically, the medical profession has been characterized by change engendered by an appeal to reason As new instruments, techniques, information, and ideas come forth, physicians are wont to change, revise, modify, or abandon diagnostic approaches and therapeutic methods Yet the road from purgation to penicillin has been strewn with the debris of intellectual, ofttimes biased, struggles to find the truth Look at the concepts of disease which have been drastically changed in the last 200 years B D Paul[4] said the following 'To work effectively with people, we must not only be able to see the world as they see it, but must understand the psychological and social functions performed by their practices and beliefs The threads of health and illness are woven into the sociocultural fabric and assume full significance only when perceived as part of the total design Internist W B Wood Jr[5] made the following statement 'Indeed, medicine can perhaps best be defined as a study of interaction of man and his environment The important environmental variables that influence his well being include not only the physical and chemical forces but social forces as well"

The culturally dependent nature of concepts of disease is well illustrated by the Navajo attitude toward congenital dislocation of the hip, a condition which most people in the United States would classify as a physical and social disability requiring medical intervention However, Walsh McDermott[6] and his associates report the following 'In Navajo culture congenital dislocation of the hip, even when bilateral, is not viewed as a disease or even as a particularly important disability Indeed, the fact that one child in a family has congenital hip disease appears to be regarded, not quite as a positive blessing, but a sort of continuously visible relative blessing By this is meant a blessing in the sense that when evil struck the family, this was the worst it could do, and evil is not apt to strike one family on too many occasions'

The modern broad concepts of human disorders noted previously are far removed from the nosology of Carl von Linne, of the 18th century Linne's concepts were based, not on causal factors, but on signs and symptoms For example the class of exanthemata was characterized by fever with spotty skin eruptions, and class 2 critical fevers were described as febrile illnesses wherein the urine showed a red sediment Newer and changing concepts of disease, as exemplified in those expressed by Paul and by Wood, are to be expected in a free, dynamic culture which must come to terms with an ever increasing flow of new knowledge The tempo of change is now so fast that one wonders how much people can afford to indulge in prejudicial thinking, which in the end necessitates the expenditure of valuable time in the arduous tasks of eliminating prejudice in order to see fact

This, then, is the new era of medicine, borrowing as in the past, knowledge, techniques, and instruments applicable to alleviation or prevention of human suffering from ever expanding disciplines With the increasing expansion of knowledge and techniques, one can hardly predict which special skill, aptitude, or unique knowledge will be required to render adequate medical care, to investigate new applications, or to teach future physicians The variable picture of future human problems and the increasing technological stream promotes a rapidly moving, dynamic mood to medicine A quick glance at the present scene seems to reveal that medicine needs the help of appropriate disciplines, nonprejudicial disciplined thinking, and an objective appraisal of our operative concepts to elucidate the basic mainsprings of flexible social attitudes

Psychology of Prescription

The future problems lie in the shadows, but there can be little doubt about their complexities The new face of physicians neither can be nor should be minutely sculptured How are future physicians to be selected? Perhaps physicians labor under an operational concept which I call the psychology of prescription It is quite natural for physicians to prescribe, and hence they are apt to lay down a prescription of courses intended to shape a person for a career in medicine The psychology of prescription has a strong hold on the medical mind, perhaps stronger than in any other profession, and its application can be seen in the requirements such as those for admission to medical school, licensure, and certification by specialty boards

Indeed, today, the clamor of the should-ers and the ought-ers is heard in the compounding rooms "You should have added a course in Sylleptic Variables" "You ought to have included some material on Glossopathy and Episodic Epistaxis for premedical students" In such proposals there is usually no correlation between veracity and the decibel level

There is, as practiced, a self-proving proposition in the psychology of prescription On examination, ingestors of the physicians' prescription can perform adequately within the confines of their value systems, that is, they have learned to act, think, and give the same answers as the physicians But this hardly proves the worth of the system It cannot be stated with any conviction that physicians in the United States critically examine their own value systems or myths with the same energy and enthusiasm that they give to the task of compounding educational prescriptions If credence be given to the view that the needs of medicine in a complex, fermenting culture will be diverse, then the physicians' exclusive authority to write the single prescription must be abandoned Admission committees may gradually come to evaluate the individual applicant and to judge him by his capacity for growth toward maturity and responsibility, his flexibility to cultural content and behavior, and perhaps special knowledge of a type which would not, today, be considered unique in terms of present medical needs As Prof H A Larrabee[7] stated, medical schools do not want science sharks, skillful technicians, deft manipulators, or winners of high grades in a list of science courses

It may well be beyond the functions of an admission committee to manifestly point out the manner in which persons should be prepared before coming to the dissecting table and the bedside The assumption that generally educated, flexible, socially oriented, mature, responsible persons with diverse talents are wanted ought to be enough However, it might be suggested that three rather general and broad considerations be explored for preparation of the applicant These are the preservation and promotion of curiosity, the fostering of creativity, and the indoctrination of rules of ethical conduct

At times, there seems to be an attempt on the part of the present educational system, deliberately or unwittingly, to smother and snuff out the natural curiosity of the young, inquiring mind This may well be an unintended result of an educational philosophy which is geared to the performance levels of the greatest number of students All too often the teacher has the necessary devices to measure performance the eliciting of answers to questions intended to ascertain the students cerebral digestive levels Curiosity, to be brought to fruition, must be directed by skill in asking questions and in the freedom to ask them The neurosurgeon Russell Meyers[8] said the following "It seems clear that without the capacity to ask the questions by which we may probe into the basic assumptions of our own cultures and subcultures and those of others, the transmission of ever-increasing masses of technical data to our pupils promises but trivial advantages Could the presence or absence of this factor—skill in asking questions—make the difference between succeeding or failing to put a satellite into orbit?"

The fostering of creativity and its ubiquitous hand-maiden, curiosity, requires a sympathetic circumstance and a self-correcting method of ascertaining the "truth"—truth not in the sense of eternal verities, but in the sense of tentative truth, subject to revision, i e to be looked at again and again Such is a formulation of the scientific method, some of whose basic tenets are (1) statement of the question, (2) collection of data by experiment, observation, and statistical analyses, (3) arrangement and classification of data, (4) tentative generalizations, (5) collection of more data, (6) revision of generalizations The universality of scientific method is not generally recognized, and there is a popular conception that it belongs in the laboratory It can and should be used in solving all problems related to human activities

One hears expressed much fear that science will gobble up the humanities, the arts, and other fields, visions of a cold, hard world depleted of emotions, human understanding, and sympathy are painted Novelists and others seem intent on preparing future generations with grim fantasies of an impoverished, mechanistic life Perhaps there is confusion here between the technology of science and the basic methods of science, the fruit is so plentiful that the tree is obscured An economical, self-adjusting method of truth-seeking could be detrimental to the humanities, the arts, and other fields only if precepts of ethical conduct coupled with an ethical philosophy are absent It has been repeatedly pointed out that no person can operate without using a sort of metaphysics and beliefs of ethical conduct The ethics of science have been succinctly described by Meyers[8] as "a preference for truth measured by the yardstick of predictability, reposing *authority in the predictive content of statements* rather than in a person or group, a readiness to share information freely with all interested fellow men regardless of race, color, creed, nationality or other circumscribed allegiances, acceptance of both the right and the responsibility to pursue any investigation that does not violate the civil rights dignity and overall psychophysiologic integrity of his fellow men, and a readiness to alter or surrender current convictions whenever demanded by empirical data that cannot be reconciled therewith " There is much to recommend that students be made thoroughly familiar with the methods and ethics of science

Art of Medicine

Science, method, and philosophy give high promise of the capability of people in the United States to effect a mature, stable culture wherein the finest rational formulation of social structure can be achieved In this culture I see not the suppression *of the art of medicine but, rather, a new high point* in its development With kind appraisal I look back at the medical forebearers in the United States realizing that their paucity of knowledge was used in a fine artful manner There seems to be, at least in my mind, a picture of the complete physician practicing proportionately with science and art When science was low, art was high, they complimented one another There has been great refinement in the instruments of diagnosis such as the electrocardiograph, the electroencephalogram, spectrographic analyses, and radioactive isotopes and in the therapeutic area scientists now use discoveries such as radioactive materials and ultrasonic sound Science advances steadily and surely and has reached the point where mechanical diagnosis with *the aid of electronic instrumentation is a practical* reality

What are the implications of this newest achievement? Does it mean that one side of the equation is all science and the other equal to zero? Does it mean the physician will step aside and let the robot do his work for him, as medical satirists have predicted? This "mechanical utopia or "mechanical hell —which it is depends on one's tastes—is hardly the end of the road The real importance of this *technological development is the enhancement* of the art of medicine Freed from the arduous drudgery of the minutiae involved in diagnosis and treatment, the physician will have the time and energy to address himself to the basic issues in such areas and perhaps, more importantly, to devote himself to his true vocation, which is to aid effectively, sympathetically, and with rapport other human beings in distress The proportion of science to art will give way to a broader expression of medical science and the art of medicine The complete physician of the future, aided by robots, will, more scientifically and more artfully than ever, care for his patients

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MEDICINE'S ATTRACTIONS AND DETRACTIONS

LOOKING TOWARD TOMORROW'S MEDICAL STUDENT

C Henry Kempe, M D, Denver

In looking toward tomorrow's medical student, the medical profession should examine present day medicine's attractions and detractions Physicians involved in medical education, representatives of organized medicine, and society as a whole are intimately concerned with what the future holds in regard to medical manpower and its quality There is much tangible evidence that organized medicine is concerned about medical education Student loan

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From the University of Colorado School of Medicine

Read before the 56th Annual Congress on Medical Education and Licensure Chicago Feb 8 1960

funds sponsored by medical societies, financial aid by practicing physicians to medical schools through the medium of the American Medical Education Fund, and annual conferences such as the ones sponsored by the American Medical Association bear this out Organized medicine is aware of the serious financial problems faced by many medical schools, which interfere with any possible lowering of tuition and prevent provision of adequate assistance to medical students through sufficient and realistic loan funds and scholarships The Council on Medical Education has suggested that at least 10 and perhaps 20 more medical schools with an average enrollment of 100 students are needed in order to keep up with our population boom These matters are of legitimate interest to any group of public spirited citizens, and physicians have no monopoly in considering and planning for future human resources in the field of medicine Although most physicians would admit that many groups have a justified interest in the future physician, some would love to keep it a family affair Alan Gregg has wisely said the following "Professionally, doctors resemble dictators alternating between complete disregard of criticism and exquisite sensitiveness to it Operating in an atmosphere of crisis met with confidence, we naturally develop a singular insularity of view, a sort of professional exemption from challenge and education at the hand of healthy and disputatious laymen We behave as though we were a group set apart, and that attitude degenerates into a kind of professional provincialism"

In considering the attractions and detractions of medicine as a career, it is important that we, as physicians, do not readily assume that our own judgments at this time in our medical life are of equal importance to those who are to follow in our footsteps For example, many mature physicians decry certain aspects of modern medical life Among these are the wealth of paper work and the innumerable insurance forms thrust upon us, some loss in the degree of freedom in which we can conduct the affairs of our hospitalized patients, and many important social and economic factors which seem to loom large to established physicians but which, we are surprised to find, are of no interest to college students who are considering medicine as a career We have yet to find an applicant who has expressed concern about the possibility of changes in the economic structure of medical practice or the fact that the tissue committees in hospitals concern themselves with our operative habits

Medicine's Attractions

Most of medicine's attractions have persisted virtually unchanged for thousands of years Medicine remains a vocation for persons possessing an intense desire to relieve suffering and to prolong life Over the centuries, the profession has had great personal prestige, honor, and considerable economic security An outstanding feature of medical practice lies in the remarkable degree of freedom and independence which guarantees virtually any physician that he will remain his own boss It still remains a field of choice for the person who is intent on making his own decisions While many practicing physicians might want to change a specific field of interest within medicine, very few are sorry that they entered medicine in the first place There is such a tremendous variety of activities open to the physician that, even if his original intent and scope of interest have changed, it is still possible within the boundaries of the profession to adjust his activities so as to find an acceptable place for himself For example, the young man who originally professed great love for his fellow men and thought he would do well in close personal relationships, in the course of which he would give direct patient service on an hour-to-hour basis, may discover that he is not so fond of people He can still switch his attention to activities in medicine or in medical research where he will not need to encounter patients or, indeed, many persons at all

Additional attractions lie in the academic and practical phases of medical training The academic program is a challenging one, as it is based on a carefully planned university background leading to an intellectually challenging career in which opportunities abound The scholarly university approach can become the lot of any physician who regards his educational experience, premedical and medical, as just the first stage in a continuing learning process Expanding research opportunities in medicine have recently made the field a wider and more challenging one Equal opportunities exist in the practice of the art of medicine Personal concern with the well-being of others, the satisfaction of filling a real need in society, and concern, in a wider sense, for the distribution and adequacy of medical care all tend to be attractive goals to idealistic young minds

Tentative decisions toward medicine as a future goal seem to be made at a very early age in many cases It is not at all uncommon to have over one-third of the students in a junior high school firmly declare that they plan to be doctors There is a high drop-out rate at this level, but even a greater drop-out rate exists at an early age for the vocations of space pilot, fireman, and policeman Granted that children of this age are not very verbal in communicating reasons for their choice of profession, they soon grow up to be more verbal as medical school applicants under the persistent urging of Admission Committees, who want to know the answer to the inevitable question, "Why are you planning to make medicine your career?" This question appears to be a rhetorical one because committees tend to view virtually all of the answers with a skeptical eye

A considerable number of pediatricians who have served on medical school admission committees have been at once concerned and amused by the degree of cynicism shown by some members of the committee Verbalized idealistic motivation in medicine as a chosen career appears to be generally devalued, and one is tempted to blame some of the members of admission committees for persuading their fellows that, of all expressed motivation, idealistic motivation is the most suspected It is probably true that the expressed principal motivation of many applicants to medical school may not be equal to their subconscious primary motivation, but it is also likely that in the past 20 years a somewhat glib approach to idealism as a motivating force in medicine has tended to make admission committees underrate the importance of altruistic motivation It is all right in the privacy of ones professional circle to theorize about the possible motivation of an applicant, particularly if this interpretation is based on intimate knowledge of the person, but it is quite another thing and most harmful, when idealistic motivation is dismissed in a superficial fashion and without much evidence or suspected as being basically neurotic The hope of medical education in the future continues to lie in the recruitment of those intellectually able students whose principal motivation lies in the desire to heal and in gentle compassion for the sick,—"individuals for whom in medicine the word love has a tangible reality" If the practice of medicine becomes increasingly less personal and if physicians do not retain their sense of high calling, medicine will become a skilled trade and will cease to be a profession Positive human motivation and superior intellectual ability both are needed in order to keep medicine the attractive career it is

Medicine continues to attract those who combine considerable scientific interest and ability with concern for human beings In addition personal independence, financial and social returns, and general aspects of prestige, remain secondary attractions of medicine to this day Despite the continuity of rewards, both spiritual and material, the profession begins to compete a little less favorably with certain other fields, and physicians must, therefore, look to the detractions of medicine

Medicine's Detractions

Some of the detractions of medicine as seen by the practicing physician are the harassment posed by the tremendous workload the pressure of telephone calls, the difficulties in keeping up with the stream of new scientific advances which directly influence medical practices, neglect of family, friends, and self, and fatigue All of these are cited as detractions of present-day medicine by those who practice it

As a full-time medical teacher I am aware of an additional detraction, which is more subtle in nature but which nonetheless concerns me greatly That is the relationship between practicing physicians and those who are responsible for educating the medical students of the future This is an emotional matter which is generally glossed over, but I believe it has a direct bearing on the education of doctors and, therefore, on the future of medicine Gregg has said the following Would that I had the light touch to deal with so delicate a theme! Blunt handling of it would produce some of the memorable effects of massaging osteomyelitis"

Many medical schools enjoy a wonderful relationship with the medical practitioners in their vicinity Other schools encounter tenacious opposition from some prominent physicians in their community Organized medicine has assumed a direct role in the financial well-being of medical schools But doctors have also a direct stake in the morale of medical schools and in the good relationships between practicing physicians and medical teachers

Mistakes have been made and are still being made by both sides Some scientifically oriented medical teachers have tended to derate the art of medicine in their teaching The pendulum has swung from the time when medicine had very little science and much art to a time when it has a staggering amount of science and little art It is important that teachers of medicine feel a healthful respect for the difficulties and responsibilities of conducting a medical practice, and it is essential that in their relations with medical students and house officers the practicing physician be identified, in attitude and fact, not as the L M D (local medical doctor) but as the respected colleague into whom the respective medical student or house officer will turn in a short time This is a two-way street, if some medical teachers have tended to look askance at medical practice, so have some practitioners tended to derate the field of medical research and the full-time medical teacher

One little-discussed and delicate aspect of this problem relates to the need for our profession to face realistically the obligation of every doctor to the education of future doctors Antagonism between town and gown virtually did not exist at a time when professors of clinical disciplines were some of the outstanding private practitioners of medicine in the community Many of the problems in this field relate to the current dichotomy In any such struggles, regardless of immediate outcome, nobody wins and medicine as a whole loses Moreover, the medical student of the future could clearly become an unhappy pawn in these destructive and irrational conflicts

The constantly improving quality of medical education in this country has been due, in large measure to the change from the haphazard and part-time proprietary trade schools of 60 years ago to the fine cooperative ventures of full-time, part-time, and volunteer faculties in our present schools, which combine the best talents of full-time medical teachers with those of able and well motivated medical practitioners in the community, who enjoy exercising their Hippocratic obligation to teach and to support medical teaching College students who have sought counsel with practicing physicians in their communities have occasionally been puzzled by destructive town and gown conflicts, and while it is doubtful that these conflicts kept them from entering medicine, they have been surprised to see serious antagonisms which they cannot understand Mutual respect, good will, and common ideals should unite the profession Medical education and the future of medicine are tangibly hurt by those who have no use for a full-time clinical teacher and by those who picture educators as socialistically inclined and who, by fostering an active spirit of contempt and scorn for all scientific medicine, derate modern medicine Physicians can take pride and pleasure in strong, competent, and idealistic medical school faculties The control of medical school curricula, the selection of faculty members, and the determination of educational philosophies must lie primarily with those charged with the responsibility for the education of our future doctors Physicians who are able to enjoy physical proximity to medical schools can happily regard their respective clinical departments as allies in the continued mutual quest for constant self-education between colleagues and friends On the other hand, they can view a skillful clinical faculty as a naked economic and professional threat To take the latter course is destructive for all concerned

Choice of Careers—The college student who is facing a choice of careers sees the following three principal detractions in the field of medicine (1) the cost of medical education, (2) the excessive length of medical training, and (3) the fact that medicine is a "difficult" subject demanding intense effort over a long period of time Additional detractions lie in the "monastic" nature of medical education By this is meant the frequently limited range of college subjects taken by prospective medical students in an effort to focus on medicine by taking many scientific subjects and getting superior grades while foregoing some of the broad educational opportunities of the university setting The monastic nature of medical education is carried on in more intensified form in medical school, which is to the detriment of the profession Another possible detraction lies in the increasing emphasis on technology This is partially due to the rapidly enlarging scientific discoveries which constantly crowd the curriculum

Medical educators and those concerned with the problems of future manpower needs in the field of medicine and the geographic distribution of doctors have been concerned lately with the relative decrease in the number of available high-quality students The number of applicants per open position has dropped significantly, and the failure rate of medical students in the first year has significantly increased The percentage of medical students withdrawing from medical school in their first year increased from 5 5% in 1954-1955 to 7 8% in 1957-1958. The superior student, both from the point of view of motivation and performance, still remains dominant in our schools, but in view of increasing needs for physicians to keep pace with our growing population we must consider those aspects of medicine which are detractions to potential students

Financial and Time Hurdles—Some brilliant and scientifically inclined students who previously chose medicine as a field in which they could combine scientific interest with good human satisfactions and a guaranteed financial future now find similar or greater scientific challenges in theoretical scientific fields where prestige, income, and a relatively short training period have become increasingly possible The rapid development of graduate school programs in universities in the United States is attracting deserving candidates The potential medical student looking forward to early marriage and family obligations must consider the fact that 10 to 12 years of training will be required before he can begin to earn enough to support his family The cost of going to medical school (between $2,400 and $3,300 per year for four years) is considerable, especially if one considers that, after this period of expensive training, there is an additional three to five years of hospital training in which accumulative debts continue to grow larger The only place where the feudal system persists in American life is in the salary scale of these interns and residents in our hospitals We must pay these people what they are worth in order to compete with other graduate school training programs, doing this, along with making scholarships and loan funds available, would tend to eliminate the serious economic handicaps of medicine as a career

Contrast this situation in medicine with the financial subsidy readily available in universities to graduate students of theoretical sciences who, as teaching assistants and research associates, can hope to work their way through school and arrive in a much shorter period at a goal which, from the scientific point of view, is as attractive and which is now receiving its due in terms of prestige and eventual financial return Those able young persons who are not attracted by the artisan aspects of engineering and medicine are going into other scientific fields Those who cannot financially afford the cost and duration of medical training can quickly find a berth in the expanding fields of technology and industry

If some more scientifically inclined students are lost from the field of medicine because of competition from the fields of theoretical sciences, what will happen to students whose primary motivation lies in the human aspects of medicine? Here again increasing competition from the fields of psychology, social service, and nursing is making some difference These disciplines recruit able students, some of whom would make good doctors but who cannot face the financial and time problems of a medical education They look forward to similar human satisfactions in these related fields

What can be done about the financial and time hurdles of medical education? It is unrealistic to hope that the present trend will reverse itself as a greater number of college students become avail able as potential medical students The probability is that the cost of medical education will continue to increase, and the percentage of married students will continue to increase and will surpass the present 60% There seems little doubt that some definitive planning for scholarships and loans to medical students will be needed to enable young people to finance a medical education without going hopelessly into debt

Success of Students in Medical School—It is not only excessive length and great cost of medical education which presents a formidable detraction Even if the tremendous economic and time burdens of medical education could be lessened—there is some hope for the former but little chance for the latter—there would still remain the inevitable problem of the demanding, difficult task of success in medical school as an academic discipline It has been fashionable in the past for medical schools to blame the inappropriate preparation in high school and college for the shortcomings of students in medical school and for their poor work habits This is too easy an explanation We must look at the entire contemporary high school and college experience and at our gadget-ridden, plush way of life in order to formulate some explanation Premedical and medical education is hard There is no evidence that many college students seek out the hard by choice, taking their example from a society whose way of life has gradually slipped from an ideal embodied in self-righteous, hard-working rigor in which virtue and hard work were equated to the present self-indulgent, lax days of spectator sports, luxury items, and a set of social, business, and personal moral values which take the "here today, gone tomorrow" point of view

The tremendous increase in enrollment in colleges depends on many economic, social, and moral factors College is rapidly becoming an automatic sequence to high school—everybody goes The reasons for going to college are no longer principally related to obtaining a first-rate, rigorous education but more often to the fact that a college diploma seems to be very desirable in the economic future of any young man or woman Sending their children to college serves many parents as the best way to insure a moratorium on early marriage, another motive which is not in any way related to classical educational goals Constantly enlarging college classes will not automatically insure high quality candidates for medical school The well-motivated, hard-working, and intellectually receptive students are frequently in the minority on the college campus, and it is from this group mainly that future doctors must be recruited

Public's Reactions to Doctors—In these past 20 years the physician has become increasingly an object of critical appraisal—frequently too critical—from the point of view of his economic and social aims and motivations Nothing has changed in the basic motives of doctors, but the reaction of the general public to doctors has undergone some change for the worse This may well have occurred in connection with the markedly reduced civilian medical manpower available during World War II During that period, under the sheer stress of time demands, the current trend toward more impersonal medicine fully emerged While children and college students of 40 years ago remember family physicians serving family needs as trustworthy counsellors possessed with reassuring skill, patience, and time, youngsters growing up in the past 20 years are more apt to have a mental image of a busy and harassed physician, pursued by telephone calls, who has shorter time intervals available per patient and who appears to be generally preoccupied with medication and getting around to the next patient in the crowded waiting room Many families frequently voice resentment over the total cost of medical care To what extent these changes in the image of the physician on the American scene have influenced the motivation of young people going into medicine, no one can tell

Altruistic Motives—Physicians must rededicate themselves to the altruistic motives in medicine Continued failure to stress the idealistic motivation of medicine to possible recruits in high school and college will tend to discourage those able young men and women who desire a fairly idealistic motivation in entering upon life's career Medicine needs to rekindle unashamedly those aspects of medicine which have no bearing on our present preoccupation with economic and political concerns Cynicism about idealistic motivation pervades our high schools and colleges Cynicism has no place in medicine, and physicians, by setting examples, must in all of their acts embody the ideals of selfless service to others and true devotion to their professional ideals

Suggestions for Improvement

What can we, as physicians, do about medicine's detractions? Medicine is unlikely to get any less hard, and medical training is unlikely to get any cheaper or any shorter The answer is four-fold We can help immediately by starting scholarships and by improving realistic loan funds to medical students We must alter the expensive character of house officer training by paying interns and residents what they are worth so that at the termination of the formal four year study they can begin to make a modest living We must reaffirm our belief in the art as well as the science of medicine by urging medical scientists and teachers to better appreciate those who practice good medicine in the community We must as a profession, defend medical scientists and teachers against unwarranted attacks by physicians who would turn back the clock We must provide an exciting challenge to the superior future students of medicine, lest we lose some who are prepared to work hard to even more demanding theoretical scientific fields where they are so desperately wanted

Nothing has changed in the great attraction medi cine holds as a career for those who combine scientific curiosity with wholesome motivation to relieve suffering and heal the ill. Personal independence and secure social and economic rewards remain the lot of future doctors.

Rapid advances in medical science are making the practice of medicine infinitely more difficult but more rewarding from an intellectual and human point of view. Medicine's increasing complexity will demand increasing selectivity in recruiting doctors. We cannot afford to focus only on the well-motivated but intellectually underendowed college student, and we must, therefore, be prepared to actively compete at the high school and college level for the intellectually able and well-motivated candidate who has good working habits and who can see medicine as a great professional and human challenge. Above all, medicine needs enlightened and courageous leaders who are not afraid of the future and who regard change and development from a mature point of view which is at once understanding, critical, and friendly.

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RESPONSIBILITY FOR RECRUITMENT

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Many studies have been made during the past years that give information on the basis of which it can be decided whether or not there is a need for a recruitment program for medical students. These studies are concerned with the future need of the nation for physicians. There are also broader studies of the educational system of the United States comparing its effectiveness with systems in other nations of the world. While research in these matters has been going on for some time, there is no question that Sputnik has popularized them and stimulated them.[1]

The Need for and Problems of Recruitment

In the year 1948-1949 there were 3.62 applicants for medical school for each freshman accepted in the medical schools of the United States. By the year 1958-1959 this ratio fell to 1.86:1. This was the lowest the ratio had been for at least 20 years. In 1939-1940 the ratio was about 2:1. In the same 20-year period the number of first year students admitted to medical schools had increased by 2,400. During the same period of time the number of graduates from medical schools increased by 1,766.[2]

These figures are of little significance unless it can be determined how many physicians are needed today and how many will be needed in the future. In spite of an increasing population and an increasing number of admissions to the freshmen classes of medicine, fewer college students are becoming interested in medicine in proportion to the number of places available in medical schools.

Most studies prognosticating future needs in medicine are based on the physician-population ratio. The use of this ratio is open to criticism, but at present there is no alternative. There has been little change in the ratio over the past decades. At the same time, "The demand for medical service has been approximately in equilibrium with the supply."[3] Using this ratio, then, seems satisfactory for the present and is acceptable until some better criteria can be discovered. Thus the prediction of the study groups that by 1975 the number of students graduating from medical school must be increased to 9,000 or 10,000 annually if there are to be enough physicians to meet the needs of the nation is a matter for concern.[4] If there is no change in the present attrition rate in medical schools during the next 20 years, about 11,000 students must be admitted to medical schools by 1970-1971 in order to produce this number of graduates in medicine. The number of admissions must be gradually increased over the next 10 years by 3,000 students. Over the past 20 years, the number of first year medical students was increased by 2,400. There is some doubt that another 3,000 will be added during the next 10 years. In spite of an increasing college population there was a decrease in the number of applicants each year in the succeeding years of 1956, 1957, and 1958. In 1956 there were 15,918 applicants for medical school, in 1958 there were 15,170 applicants, a drop of 748 college students who were interested in a medical education. This certainly indicates that there is a job to be done.

Other problems indicate that something must be done. Medicine has always demanded and has always received the upper level of mental ability among those graduating from the colleges of the nation. In order to maintain the present high quality of students and physicians, medicine must continue to draw its students from this college group. However, medicine is facing increasing competition for these same college students.[5] As the world progresses further into the age of technology, this com

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petition will become more serious Engineers, scientists, and educators are looking to these same superior college students for their future leaders The nation's future depends on this type of student in these nonmedical professions Formal campaigns have already been instituted to attract these students away from medicine

There are just so many students graduating from the colleges of today who can meet the demands for intelligence of medicine, science, engineering, and education With the increasing population there will, of course, be a proportionate increase in the number of this type of student But because this age is technological and demands more and more nonmedical scientists, engineers, and teachers, proportionally fewer students will enter medicine even though an increase in population will necessitate an increase in physicians There will not be enough gifted students to satisfy all these professions Medicine must develop some plan to attract its required share of these superior students

These facts demonstrate that it is not a mere assumption that a recruitment program for medical students is needed In the development of such a program the medical schools should first list their assets, then their supply of raw materials, and finally their debits or deterrents They must plan their programs to exploit their assets, to increase their supply of raw materials, and finally to liquidate their debits

Assets of the Medical Profession

The assets of the medical profession are well known prestige, reward, freedom, challenge, and satisfaction in service to mankind There are no doubt many others, but none of these assets are of any value in a recruitment program unless they are made known to those whom the medical schools desire to recruit The students in the secondary schools and colleges must be educated and reeducated concerning these assets Their parents must be made aware of them The program must be carried out by all segments of the profession

The individual practitioner of medicine has been told time and time again that, by the very conduct of his practice, he can better provide public relations for the profession than all the high-cost public relations programs conducted by state and national medical organizations He must again be told that he holds in his hands a most potent means of preserving the high quality of the physicians of the future By the manner in which he conducts his life, by his participation in civic and community affairs, and by the quality of the medicine he practices, the prestige of the medical profession is determined He should take an active part in the career day programs in his local high school He should exercise his duty as a citizen, serve in public office when called on, and exercise his good judgment in supporting good public servants In short he must always be a good doctor and a good citizen of his community

Organized medicine has its role to play in building up the prestige and the opportunities of a career in medicine It should establish for itself a reputation at all jurisdictional levels as a responsible organization for advice on policies and practices concerning health Health fairs, career day programs, and science fairs should be promoted by county, state, and national medical organizations Such programs should be planned so that they present to the people, both young and old the past accomplishments of medicine, the future possibilities, the variety of the field of medicine, and both the material and spiritual rewards of medicine Organized medicine should demonstrate an objective interest in insuring a high quality of medical care to all people regardless of economic status It should concretely demonstrate an interest and a willingness to accept its responsibility in overcoming the deterrents to a career in medicine

Medical schools and medical research facilities should accept their responsibility to inform high-school and college students of the advantages and attractions of medicine as a profession As an example as to how this might be done attention should be called to the grant-in-aid fellowships in medical and dental research awarded by the Georgetown University Medical School to selected junior and senior highschool students[6] These $100 fellowships for experience in medical and dental research, as a part of an actual research team, cannot help but inspire the recipient to further direct his course toward a career in medicine or dentistry The faculty of medical schools should be willing to participate in high-school career day programs and in college premedical and scientific society programs, in fact, they should seek out such participation Close and friendly relationships should be cultivated by medical schools with high-school counselors and college premedical committees Indeed there is a broad role that medical schools might play in this phase of the recruitment program Since they need the student they must share in the responsibility of recruiting the student

Improving Elementary and Secondary Education

In order to deal with the problem of the limited source of supply of students for medical schools and the increasing demand on this source by other professions, it is necessary to determine how this source of supply can be increased to meet the demand for physicians and what role liaison at all levels of education with medical schools and the profession of medicine might play in the solution of this problem According to Adm H G Rickover[4a] and others, about 6% of the fifth grade pupils in the United States pursue education to their doctorate degree He estimates that in Russia 10 to 12% of this same age group complete their postgraduate education Why does this percentile difference exist between the youth of the United States and the youth of Russia? Is it because the children in the United States do not have the mental ability or capacity of the Russian children? This is doubtful It can be readily assumed that they are equal in mental ability and capacity If that is true one can only come to the conclusion that the American elementary and secondary school system is less well adapted for the gifted children than comparable schools in Russia Most European school systems seem to be able to get their children through the college preparatory courses in greater number and in fewer years than the school system in the United States In most instances it is unfair to pit the United States high-school students against the European college preparatory students in an examination used for such students in Europe The United States would fare better by using United States junior and senior college students against the European high-school student in such an international contest

According to Admiral Rickover [10] the educational system in the United States has not been geared to "*seek out and identify our talented children In most schools they are being taught along with the 80% of average and below average mentality, although there is some selection through the elective system* Only those with good minds are apt to take the academic college preparatory program Unfortunately, not nearly enough of those who can master such a program actually select it Very little provision is currently being made to take into consideration the fact that talented children learn much faster than others Consequently, the length of time spent in school is the same for almost all children

"There is ample evidence that in any class which includes slow and fast learners the slower group sets the pace and receives more attention from the teacher The above average children are kept from advancing at the speed appropriate to their ability, with the result that some lose interest in learning as such, others develop sloppy habits, and a few build up a false sense of superiority which convinces them that they are so smart that they will never need to apply themselves to anything The deadly routine sets in on these young and malleable minds

"Talented children whose minds are not challenged become frustrated and often turn into poor pupils from sheer boredom Mental muscles become flabby if the child's mind is not constantly being strained to the utmost The mind is no different from any other part of the body It deteriorates when it isn't used for its proper purpose—to think"

What does all this mean? It simply means that there is a definite need for improvement in the elementary and secondary educational systems Such improvement has the potential to make, in fewer years, up to twice the present percentage of the school population prepared and anxious to acquire advanced degrees in the sciences, medicine, engineering, and education

Therefore physicians must participate in a movement already started to improve the entire educational system of the United States At the elementary and secondary level, education is largely locally controlled The medical profession must participate in this control by taking an active part in the parent-teacher associations, seeking election to school boards or insuring that well-qualified fellow citizens, dedicated to improvement in education, are elected, and making strong efforts to improve the quality of the teachers in these schools Less money should be directed to elaborate school buildings and equipment and more to teachers' salaries Locally, everything should be done to elevate the prestige of the teacher These two efforts would do much to attract to the teaching profession men and women who have the ability to implement and carry out a type of education geared to the intellectual ability of the individual student It is this type of education that will bring the talented student to medical school at a younger age, with greater motivation and maturity of mind

Improving Medical Education

The factors which deter students from the study of medicine are not hard to find, and most of them can be corrected One of these deterrents is the long course of education necessary before the student becomes an income producing member of the profession Every time I hear this subject discussed at medical meetings one more year is added to the total medical curriculum It is high time we reevaluate our medical educational program the premedical preparation, the undergraduate medical course and the postgraduate programs

Is there good coordination of philosophy, objectives, and implementation between premedical preparation and the undergraduate medical school? Are medical schools duplicating courses already given in premedical college? If the quality of teaching in premedical colleges were raised and standardized, could some of the basic sciences be transferred from medical school to premedical college? Or should the extensive scientific preparation presently provided by the premedical colleges be discouraged and the curriculum be shortened? At the Dallas meeting of the House of Delegates of the American Medical Association, resolutions were approved encouraging and urging medical schools to include in their curricula courses in medical sociology and economics Could such courses not be adequately presented as a part of premedical preparation, rather than in the medical school? By establishing close liaison between secondary schools, premedical colleges, and medical schools and by creating an improved elementary and sec ondary educational system, could medical schools develop an over-all curriculum that would give the prospective medical student a broad background of training in the humanities and the basic principles of science in less than the 16 years now required prior to entrance into medical school? Are medical schools teaching obsolescent facts and procedures which might well be eliminated, as was suggested three years ago at one of these Congresses by Dr Oliver Cope? [7] Now that all forms of medical practice, from the general practitioner to the most limited specialist, require postgraduate residency training, are we making too great an effort to produce a finished product in the undergraduate medical school? Is the internship necessary today, sandwiched between the clinical clerkship and the residency? Is the present trend to continually lengthen the specialty residency training program sound?

Many of these questions may sound ridiculous and probably are On the other hand the rigid adherence to a four-year undergraduate medical program might be just as ridiculous in view of the great changes that have taken place in the methods of education and the methods of practice during the past 25 years Research in education has been most dynamic Medical school faculties are to be congratulated for what they have accomplished and for what they are doing in the way of research in education They are turning out an increasingly improved product each year But they do have a responsibility to look at the monster they have built in this process They have a responsibility to reevaluate the whole, to amputate the unnecessary and to streamline where streamlining will not lower quality They must concern themselves with the type and quality of education in the secondary schools and colleges preceding medical school

The specialty boards should take a look at the time required for specialty training and certification As it now exists a young surgeon might be approaching middle age (he may be 35 years old) before he becomes an independent practicing surgeon Should society ever apply to medicine the arbitrary retirement at age 65 that it does to other occupations and professions and as some hospital staffs do to active membership, we will have reached a training-practicing ratio of one year of training for each year of practice Is this efficient use of our medical manpower? Is so much precertification training necessary to assure quality? How much does this alone deter the prospective medical student? He knows that with a doctorate degree in science, engineering, or education he can start his personal career at the age of 25 years, perhaps His starting income at this age may well be greater than the starting young surgeon of 35 years of age With the increasing demand for doctorates in these nonmedical professions and the short supply of such trained personnel his potential maximum financial reward may well equal, if not exceed, that of our surgeon 30 years later when the former is in his prime at the age of 55 years and the surgeon is 65 years old Certainly 10 years of life, and particularly the 10 years that occur between the ages of 25 and 35 years, are of value to the superior student He will be most careful how those years are spent and what they will purchase

Cost of Medical Education

The second deterrent is economical the high cost of medical education No one can deny that it is high, taken by itself, compared to the cost of education for our competitor professions it is indeed expensive The medical student in today's private medical school is asked to pay in tuition about one-half the actual cost of his education The remaining half of the cost is paid as a subsidization by medical school endowments and grants for medical research awarded to the respective medical schools In state medical schools there is greater subsidization These schools have the same endowments and grants as the private schools and also receive appreciable funds from state taxes

In addition to this hidden aid to financing, there exist many scholarship and loan programs for the needy medical student But such financial assistance is not enough Many qualified students cannot afford the cost of the prolonged educational course required in spite of these subsidizations, scholarships, and loans When the high-school student and his parents consider the tuition, the cost of room and board, and the living expenses necessary through the four long years of premedical college and the four long years of medical school, they may be frightened and discouraged No wonder many parents with average or below-average incomes direct or encourage their son or daughter away from medicine and into some other profession A student can work during college and through the summers and thus earn his way through college He cannot do this in medical school and get the maximum he wants and should have out of his medical education Yet many of the superior students that medicine needs are the sons and daughters of parents with little money to spare

Students and the parents of students in high school and college are well aware that in fields of science other than medicine there are just as many scholarships, loan programs, and as much subsidization by endowments, grants, and tax funds, and they also know that in the nonmedical professional schools the scholarships are better than those in medical schools Medical scholarships and loan programs are often limited to the second, third, and fourth year in medicine There is a waiting period of one year, the first year, to determine whether the student deserves the assistance Many premedical students have a difficult enough time paying the cost of their college education They want to be able to foresee the financing of their medical education for its full four years before committing themselves irrevocably to something which they might not be able to afford On the other hand, graduate science, graduate engineering, and graduate education scholarships can be secured while the student is in college, and these provide for the entire course of graduate education Loan programs in these same schools do likewise These nonmedical graduate schools also offer something in the way of easing the cost of education that is not offered to the medical student fellowship programs In addition to providing for the tuition of the student, fellowships usually aid in the living expense to a modest degree This is of particular value to married students of whom there are more each year

Medicine and the medical schools must take some steps to alleviate this financial problem Strenuous efforts must be made to increase endowments Scholarship and loan programs should be extended to include the first year of medical school They should be awarded during the premedical preparatory period A campaign to develop fellowships for medical schools, privately or publicly sponsored, should be instituted In view of the increasing confiscatory type of tax programs in existence today and their effect on possible sources of private funds for such fellowships, perhaps medicine should reconsider its attitude toward governmental support of education Studies should be made to discover if there is some method by which there could be developed government sponsored fellowships which would have no possible opportunity to destroy the freedom that is enjoyed and cherished today in the system of higher education It is fully realized that such thinking is contrary to the principles on which the American Medical Association has long stood firm, but the A M A must be realistic There is no equality of economy between the states or between regions within the respective states Yet each gifted student, regardless of his native state or region, should have the opportunity to secure the degree of education for which he has the mental ability and capacity Furthermore, in this technological age, the United States needs to develop all its brain power It cannot be penalized in this respect by the low economy of some states or regions of states If there are not sufficient private funds available to meet the needs of medical education, some use of federal funds, as a catalyst perhaps to stimulate state and local funds for this purpose, should be investigated Nonmedical graduate programs utilize such funds, and they report no loss in the freedom of their educational programs[8]

Summary

There is a very definite need for some program for the recruitment of medical students The primary responsibility for planning and implementing that program rests on the medical profession as a whole The individual practicing physicians, employed physicians, medical educators, and research fellows all have a responsibility not only in the planning but also in carrying out the program It has been suggested that the program be fourfold There should be a program to exploit the attractiveness of a career in medicine The medical profession should join hands with other professions in an effort to improve the educational system, particularly at the elementary and secondary school levels, in order to increase the number of qualified students that reach the stage in education when they are ready to enter medical school and also in order to shorten the entire premedical preparation from the present 12 years Much of the cultural education which he would now undertake in premedical college could be given to the gifted student whose education has been paced to his superior mental ability while he is in his academic college preparatory school Within the period of medical education per se, the medical educators must earnestly experiment and investigate ways and means as to how it might be shortened Finally, all segments of the medical profession must develop some means of adjusting the cost of education so that no student properly qualified and mentally able is prevented from securing a medical education because of its high cost But a most important word of warning is necessary No part of whatever program of recruitment the profession elects to implement should in any way lower the quality of the physician produced If anything, the program should include methods of increasing this quality Quality should not be sacrificed for quantity

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OBSTACLES TO MEDICAL EDUCATION AT THE INTERNATIONAL LEVEL

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Medical education outside North America is a subject of interest because thousands of foreign graduates are now coming to the United States and Canada for graduate training in the clinical sciences as interns and residents It is the responsibility of North American institutions to provide as high a level of training as possible Quite aside from the moral obligation to provide any student with the best experience in medicine for his future work abroad, North Americans have a completely selfish obligation to do so in order to assure adequate care of patients in their own hospitals Planning of such training depends on an understanding of the obstacles, better termed differences, in the training of these students at the medical school level

Foreign Education System

In view of the importance of understanding the basic curriculum followed in parts of the world outside North America in order to adjust our graduate programs to the educational background of foreign trainees, it seems appropriate to review some of the basic differences between the two systems in preparation for medical school as well as to review the medical school curriculum In general, students attend four years of primary school, four years of intermediate school, and four to six years of secondary school The students graduate from secondary school with a degree or certificate which qualifies them for admission directly to the university The time spent in preparation for university work is about equivalent to the number of years spent in grade school, junior high school, and high school in the United States Students enter a university abroad at the age of 16 to 18 years, which is about the same age for entrance to American colleges There are, however, two important points to remember in comparing the systems The foreign curriculum for the early years before university entrance is designed, in theory at least, to include all the work normally taken by American students through the first two years of college The second point is that foreign universities are graduate rather than undergraduate schools in the American sense Students therefore go directly from secondary school to graduate work as medical students, law students, engineers, and so on This system is in essence, the European plan for education, which has been most effective, with one or two exceptions

Insofar as medical education is concerned, this system is adequate where the countries themselves have in fact adhered to qualitative as well as quantitative aspects of the curriculum of the secondary school All too often, however, the quality of science education in these years is inadequate and largely theoretical in its approach Consequently, in many countries students enter medical school without the sound knowledge of biology, chemistry, physics, or mathematics which is suitable for graduate study in medicine In all countries using this basic educational system, some form of fundamental science teaching has been added to the medical curriculum in the first year Unhappily, the courses are often given by professors from other fields in medicine or are oriented to medical aspects of physics, chemistry, or biology Thus a vast number of students throughout the world start the intricate process of learning the art and science of modern medicine without the fundamental knowledge necessary to understand the complicated fields of the basic medical sciences and their application in clinical medicine

This situation is perhaps the most serious obstacle to progress of medical education in many areas abroad In almost every country able young scientists with modern training are returning to their universities with a desire to improve scientific instruction, but in many cases the students are quite unable to meet the challenge of better education because of basic deficiencies in their fundamental education

The medical curriculum generally includes seven years of study, although there is now a strong move to reduce formal study to six or six and one-half years and to add a year of practical work after the formal courses The first year is devoted to biology, chemistry, physics, and anatomy The second and third years are normally concerned with physiology, biochemistry, more morphologic science, and, occasionally, introduction to medicine In many universities the fourth year includes microbiology, pharmacology, introduction to pathology, and lectures in medicine The fifth and sixth years are assigned to medicine, surgery, and pathology while the seventh year is used for instruction in the various specialties There is always a sprinkling of other subjects such as psychology, preventive medicine, and legal medicine throughout the curriculum In view of the early age at which students enter medical school the length of the curriculum is probably desirable, and the content, in theory at least, would be equivalent to that used in North American schools As we shall see, however, there are several factors which tend to detract from the quality of the physicians produced by this system

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Associate Director the Rockefeller Foundation

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Problems of Foreign Medical Education

First, and perhaps foremost, is the problem of limitation of admissions to medical schools and the general lack of selective procedures for admission. This does not apply to such places as the United Kingdom, Sweden, Norway, or to one or two countries outside Europe. The general practice, however, rooted in a tradition of university education for anyone capable of passing from secondary school, is to accept all persons who choose to enter medical school irrespective of their academic record, personality, or motivation. Since a career in medicine has distinct social and economic advantages, it is not surprising to find that large numbers choose the school of medicine.

If the university is small and provincial one may find relatively small numbers of students entering the school of medicine. However, the large state schools almost without exception admit classes of 500 to 2,000 students annually. There have even been examples of classes up to 6,000 students. Classes of this size clearly preclude any small group teaching, intimate interchange between professorial staff and student, and, more important, any appreciable practical laboratory instruction. Instruction is largely by lectures and demonstrations to large groups of students barely able to hear the professor. Lacking practical instruction and an opportunity for discussion of the subject with the staff, the students turn to learning by rote from textbooks, often out of date, or from students' notes laboriously reproduced with the original errors and sold to less fortunate colleagues. Since in most of these institutions the students who fail are permitted to repeat courses as often as they like, the problem of a large student population becomes an overwhelming obstacle to the production of quality.

In looking over the plan of studies of many foreign institutions, one is often puzzled about why students appear to spend so many academic semesters on a given subject which may well be covered in North America by one semester or perhaps two quarters. The explanation becomes apparent when one realizes that most of the institutions have an academic year of six months, interrupted by many national and religious holidays and lengthy periods for examinations. In spite of the short academic term, most schools teach formal courses only in the mornings, even in the basic sciences. This is due, for the most part, either to a lack of tradition of full-time academic work or to low salaries which force the professorial group to seek outside income from either practice or private laboratories. Thus the student body is left to its own resources for a large portion of the school term. To prepare for the detailed and theoretical examinations they turn to textbooks or, perhaps, to sports and motion pictures.

Clinical instruction suffers from the same deficiencies. In general teaching hospitals are large charity or state institutions which are staffed by the professors and their assistants. Characteristically, the staff members attend the hospital for a few hours each morning devoting the remainder of the day to practice. Since resident medical officers are not normally employed in the teaching hospitals and since the professor and his two or three top assistants retain all responsibility for teaching students, instruction is limited to morning hours and consists of massive lectures with demonstrations of patients. Only seldom are students allowed to participate with responsibility in the examination of a patient.

For the most part, a modern clerkship of the sort that exists in North America is unknown except in the countries noted. As a consequence, students may and do pass through medical school, are licensed, and start practice (or come to North America for training) without ever laying a hand on a patient or listening to a heart murmur. In fact, in two countries of Europe which I have visited on many occasions thoughtful educators in the clinical sciences have estimated that over 70% of all the graduates fall within this category. Graduates coming here for clinical training arrive without previous practical experience in patient care and have been trained in a tradition which fails to give them the practical responsibility for patient care and diagnosis which is routine to resident staffs of American hospitals.

These obstacles and many others add up to an imposing problem in terms of graduate training for the new physician either here or abroad. Each country is attacking the problem in a variety of ways. Changes are not easy to achieve in institutions steeped in tradition and, in some cases, manned by professors who are distinguished but who have somewhat dated ideas about scientific medicine. In some of the European countries the problems of large classes and little opportunity for practical acquisition of knowledge are overcome by licensing graduates only for community practice outside of hospitals. The more competent students go on to seek an M.D. degree in graduate studies over several additional years, during which they work as a voluntary assistant in one of the clinical services, receiving each year additional practical and supervised training with patients and taking on increasing responsibility Thus a reasonable supply of fully trained specialists for hospital practice is maintained, although the quality may vary tremendously

Solutions

A new model for intensive reeducation of foreign applicants will have to be established in the United States They need retraining or refreshing in the fundamentals of biochemistry, physiology, and the related fields of mathematics, chemistry, and physics if they are to use modern clinical tools competently They must be oriented to American practices in examination and diagnosis of patients in the hospital setting and geared to a level of responsibility for patient care which will permit them to function effectively as resident house officers

A beginning has been made in this direction on a small scale Tulane University has established an intensive review course in science which covers one year This has been eminently successful but is limited to a few graduate students who are preparing to fill major academic posts in universities abroad both in preclinical and clinical fields Cornell University Medical College has operated an orientation course in the clinical sciences at Bellevue Hospital in New York City for several years The merit of the course is demonstrated by the fact that graduates of the six-month course are able to enter top teaching residencies This course is limited and is designed to prepare academic personnel While these pilot courses have demonstrated that intensive retraining or orientation is feasible and successful, they cannot serve as a pattern for the over-all problem of evaluating and orienting several thousand young foreign doctors who annually apply for and are accepted in internships and residencies in the United States

The solution is not clear A step has been taken in the evaluation of the basic knowledge of applicants by requiring certification by the Educational Council for Foreign Medical Graduates In this program students are required to take a modified form of the National Board examinations This gives a reasonable measure of the technical knowledge of the students, which even in the poorest schools may be substantial if the student has a good memory and has probed the textbooks at length It does not, however, measure the capacity of the student to manage patients in the course of an internship or residency

I suggest that the hospitals, either alone or in groups, will have to take the ultimate step of providing training through clerkships under supervision, combined with a review of basic science along the lines adopted by Cornell University Medical College, before assignment of medical graduates as house officers In the end, this will improve materially the medical care supplied by the hospitals, provide a better basis for graduate teaching of all the house staff, and, most important of all, raise the standard of graduate education of foreign students who have honored the United States by applying for training in its hospitals and schools

111 W 50th St (20)

MEDICAL SCHOOL SERVICE —This service was first established in the Out-Patient Department in 1905 It was the inspiration of Dr Richard C Cabot the objective being to provide a medium by which the recommendations of doctors for the treatment of their patients could be better carried out Treatments as recommended often meant increased expense family adjustments, social problems and even operation or drug therapy which needed explanation and supervision Begun in a small way, it soon demonstrated its usefulness and spread to the wards and ultimately to private patients At first directed and financed by a separate organization, it was accepted by the Trustees as an integral department of the Hospital in 1919 It has always been considered as an aid and adjunct to medical treatment, not an administrative department dealing with the financing of admissions and hospital care The success of Social Service at the Massachusetts General Hospital led to its spread and acceptance by hospitals throughout the United States and Canada —N W Faxon, The Massachusetts General Hospital, 1935-1955, Cambridge, Mass Harvard University Press, 1959, page 227

PUBLIC HEALTH ACTIVITIES OF A COUNTY MEDICAL SOCIETY

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The experience of this county medical society shows that a public health committee can be extremely effective in dealing with many local community needs The parent committee has been in a position to call on members of the society to help communicate the message of health to people in public meetings, radio broadcasts, newspapers, and programs arranged by nonmedical groups A plan for periodic health examinations for physicians themselves has been carried out, important legislation has been obtained, a directory of medical and social services is in preparation, and many special health problems have been investigated Subcommittees have been successful in encouraging immunization against poliomyelitis and in organizing campaigns for mental health The results of these sometimes laborious efforts have amply justified the expenditure of time and energy

The private practitioner little realizes the extent of his contributions to the field of public health and community hygiene Medical historians recognize that these contributions have added considerably to public health knowledge The current literature gives further evidence of these values[1] The potentialities are still greater when individual efforts are channeled through organization and keyed to the unique status of the private practitioner in the framework of medical practice His closeness to the patient, his knowledge of his patients' problems, and the goals he wishes to obtain for them help toward an immediate, vital, and realistic contribution Organized medicine, being the sum total of all practitioners, can translate these efforts from the source initiate and organize a program of its own, and throw its weight toward cooperation with public and voluntary health agencies

The public health committee of the Medical Society of the County of Kings, during the last four years, has been organized toward this goal What has been done at Kings County can be done elsewhere, given vision, encouragement, and leadership

The public health committee is a cross-section of the membership of the medical society Members of the committee include general practitioners and representatives from different specialties, including public health This union of many disciplines gives the committee a broad concept, a wide experience, and a deep insight into the problems of the patient and community With this background, there is a fresh point of view in handling public health problems Participation of the entire profession in public health programming has been strengthened By the same token, the specialists in public health of the committee have contributed greatly by sharing their experience and background with other members

It has also been recognized by the committee that the practice of public health includes more than a single medical specialty, and so it has used the experiences of nomedical men by having as consultants to the committee an expert in the field of statistics as well as one who is a specialist in the field of public health education

In planning and effecting its program, the committee has had the confidence and support of all the officers of the society, as well as the Comitia Minora During the last four years, each president of the Medical Society of the County of Kings has given the committee and its chairman his unqualified encouragement and support. A key feature of the programming of the public health committee is its close cooperation with the Brooklyn office of the New York City Health Department This bond is exemplified by the appointment of the borough health education coordinator of the department of health as consultant in health education and public relations to the committee

Services

Poliomyelitis Vaccine.—The need for accelerating the poliomyelitis inoculation campaign at a community level was recognized by the committee in the fall of 1956 Parochial schools and child-care centers were singled out for an intensive drive Inoculations were started in Dec, 1956, at a local community house which had a large preschool attendance The department of health issued Salk vaccine without charge, and members of the Kings County Medical Society donated their services This initiated a cooperative venture which contin

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Read before the Health Officers' Section at the Annual Meeting of the American Public Health Association, Atlantic City, N J, Oct 19, 1959

Chairman, Public Health Committee, Medical Society of the County of Kings, and Borough Chief, Bureau of Preventable Diseases, Department of Health (Dr Lichtman), and Borough Health Education Coordinator, Department of Health, and Consultant, Health Education, Public Health Committee, Medical Society of the County of Kings (Mr Podair) ued for one year during which time the campaign spread as a drive for mass immunization of adults also These drives spread to colleges, community houses, housing projects, parent-teacher groups and commercial organizations The vaccine was administered without charge to college students and residents of low-income housing projects, and for a nominal fee to those who could afford to pay During the drive, 16,839 innoculations were given

The second phase of the poliomyelitis program was an educational one News releases were sent to all local newspapers pointing to the urgency of immunizations for both children and adults Posters urging immunization were made available These were distributed to each member of the Kings County Medical Society for his waiting room

Mental Health—Community mental health has become a public health problem of the first magnitude Its facets are so many and diverse that individual efforts cannot hope to solve them The only hope of finding a solution lies in the coordinated efforts of dedicated people in the medical, public health, social, and political sciences

The public health committee, recognizing the need for the union of minds and experiences of medical specialists who work daily in this field, formed a subcommittee for mental health In 1957, the subcommittee grew from 1 member to 50 members, all of whom were practicing psychiatrists in Brooklyn Subcommittees were formed to study such problems as child mental health, emotional problems of the aged and chronically ill, addiction and alcoholism, juvenile delinquency, education of the nonpsychiatric physician, psychiatry in the general hospital, epilepsy, mental deficiency, and forensic psychiatry

Psychiatric training for the nonpsychiatric physician was considered one of the first steps necessary in developing a community mental health program, and in the fall of 1957, with the cosponsorship of the Brooklyn Psychiatric Society and the Kings County Chapter of the American Academy of General Practice, a series of seminars was inaugurated on subjects in the field of mental health which would interest the practicing physician The seminar technique was used because it was believed superior to the didactic lecture method in postgraduate education The old preceptor principle coupled with those modern techniques employed in group therapy was used

Each seminar was led by a member of the subcommittee, a practicing psychiatrist, with six to eight physicians participating It was held in the evening, in the psychiatrist's office These seminars proved popular, and lay people requested participation Many hospitals are experimenting with this method for their postgraduate training

This year, nine subjects are planned for the seminars The Brooklyn Psychiatric Society, the Brooklyn Academy of Pediatrics, and the pediatric section of the Medical Society of the County of Kings will cosponsor one group of seminars on the psychiatric problems of children

The subcommittee has also inaugurated a free consultation service for the members of the Kings County Medical Society who may call on any member of the subcommittee for advice concerning any psychiatric problem which is encountered in practice

Methods of Communication

The Physician—Physicians have always used health education as an adjunct to therapy Understanding a difficult situation which confronts the patient or family group has always given the doctor an opportunity to clarify and interpret the nature of disease As he is close to the patient, he can acquaint himself with the patient's attitudes, fears, and hopes His study of the nature of the disease process gives authority to his considered opinion To practice his profession most effectively, he must have cognizance of the progress of medicine

The public health committee has used to great advantage these unique qualifications by calling upon members of the society to help communicate the message of health to the public The rationale behind the program of public health education is to educate the public and to correct misinformation that is presented by nostrum peddlers through radio and television, by quacks from the public platform, and by misguided newspaper articles on health

Forums—The Brooklyn Institute of Arts and Sciences, known locally as the Brooklyn Academy of Music, supplied the first platform for our efforts in the form of a lecture hall which seated 400 people A mailing list of 15,000 of their members and publicity in their monthly and annual brochures helped increase attendance

From 1956 to 1957 our program was entitled Twelve Wednesdays for Your Health Two speakers and a moderator took one hour for their presentation for each program After this, one-half hour was devoted to questions and answers in which the public participated An evaluation questionnaire was distributed after each meeting to determine whether the information presented was useful, interesting, and comprehensible The Brooklyn office of the New York City Health Department and one of the large daily newspapers in New York City further publicized these forums A feature writer was assigned to the forum and reported the highlights to his newspaper The most important questions and answers were included in the lead column, and frequently, there was an editorial on the Brooklyn pages of the newspaper

Any local health organization interested in the topic for a particular forum was invited to participate by setting up an exhibit in the lecture hall, by distributing its literature, and by answering questions about the work done by its chapter. This gave such organizations as the Brooklyn Chapter of the Rheumatism and Arthritis Foundation, the Brooklyn Association for Mental Health, the Brooklyn Cancer Committee, and many others an opportunity to participate in and to cosponsor these forums.

This series has been continued yearly because of its public popularity. Some of the topics discussed were entitled New Frontiers of Public Health, Diabetes, Polio, Mental Health, Coronary Heart Disease, Antibiotics, Cancer, and Nutrition. The most popular lectures, as judged by audience reaction and demand, have been repeated each year.

The editor of the New York State Journal of Medicine evinced an interest in some of the material presented at the forums for possible publication. When these articles were submitted, we were pleased to note that a series of four papers were published under the caption of Health Forums in the New York State Journal of Medicine.[2]

Broadcasts.—The response to the health forums was so encouraging that the committee decided to extend its activities to meet a wider audience. With the cooperation of the radio and television unit of the Bureau of Public Health Education of the New York City Health Department, arrangements were successfully completed for radio station WEVD to carry our health message to its audience (about 50,000) as a public service. The series was entitled On the Health Front.

The format of this program was changed somewhat from that of the forums in order to create greater radio listening interest. The moderator, a member of the Public Health Committee, interviewed two doctors, specialists in their field, who answered questions previously prepared which covered the topic of the evening.

After the first broadcast, the chairman of the public health committee was told that the State Department had selected this program for rebroadcast. The Voice of America requested a transcription and used it on its overseas program. From an audience of several hundred at the forums, to several thousand over WEVD, to a worldwide audience by means of the Voice of America, was significant recognition for the efforts of the public health committee. We have since been informed that most of the broadcasts have been accepted for rebroadcast by the Voice of America.

The topics chosen included some that were discussed at the forums, as well as such subjects as aging, viruses, allergies, and heart disease. WEVD taped all programs for rebroadcast during this past summer. Many daily newspapers featured this radio series among their highlights for the day's broadcasts. Plans for the coming year include such subjects as radiation hazards, fluoridation, and venereal diseases.

Newspapers.—Many protests from irate citizens and from district health officers of the department of health were received by the chairman of the public health committee concerning cultists who were writing for several Brooklyn weekly periodicals. These cultists were viciously attacking standard public health procedures, particularly fluoridation and poliomyelitis immunizations.

A member of the public health committee was requested to discuss this problem with the newspaper publishers in order to give organized medicine an opportunity for expression which is upheld by scientific truths. It was agreed that a weekly health column written by an editorial subcommittee would be published in these newspapers. Within 10 days, eight articles were ready for publication. This column continues to be published.

Speakers.—As the level of public education rises, there is a greater demand for authoritative health information. The demand by lay groups for speakers has increased considerably in the last few years, particularly by parent-teacher groups, churches, golden age centers, settlement houses, and many other community groups. Requests have been made to the department of health and to other community resources for speakers. The difficulty in obtaining qualified speakers, particularly psychiatrists, has hampered this public service.

A speaker's panel, which was composed of volunteer physicians and members of the Kings County Medical Society, was organized to cooperate with the Borough Health Education Coordinator of the Department of Health. The list, which included the specialty of the speaker, was sent to each health educator working from a district health center. Subsequent arrangements were then made directly with the speakers and when completed the chairman of the subcommittee was notified and proper recognition was given to the speaker in the Bulletin of the Medical Society of the County of Kings. When the Medical Society received a request for a speaker, it was also channeled through the chairman of the subcommittee. This helped the County Medical Society in rendering an educational service. It also served as a source of contact for the department's health educators who work with community groups.

Other Programs

Medical Examinations of Doctors.—The principle of periodic health examinations has been advocated by the medical profession for years. Monophasic and multiphasic screening examinations, such as periodic chest x-rays, precancer checkups, and health surveys have been derived from this prin ciple Federal agencies, state and local health departments, and private welfare organizations have utilized these techniques to great advantage Many members of the medical profession, although advocating periodic examinations, often neglected to practice such precepts where their own health was concerned The profession has a further responsibility in this matter of public concern, that is, to show by example the importance of the periodic examination The physician who submits to a periodic physical examination benefits himself and also carries the sincerity of his conviction to his patients

In Dec 1956, a pilot study was undertaken to learn techniques of multiphasic screenings of members of our society by their colleagues at a county level An essential feature of the examination was its confidential nature and anonymity The study revealed many pathological conditions unknown to the person examined The need for a periodic examination was deemed essential

In the fall of 1957, a card was sent to members of the society requesting them to indicate the desire for a physical examination The enthusiastic returns indicated to the public health committee that the seeds planted by the pilot study were taking root

The facilities of the Kings County Medical Society, which had been used for the pilot study, were found to be inadequate for the number of applicants requesting examinations Cooperation of the New York City Health Department was requested The response of the Brooklyn office was immediate and favorable

Four health centers in Brooklyn were chosen for the examinations These were so situated as to be within easy reach of each doctor A history and physical examination form was developed by the public health committee for this occasion The details of the examination and the method of preserving anonymity, have been described in a previous paper[3]

The results of the examinations of 235 doctors and the publicity of the campaign in the lay periodicals were very gratifying and justified the laborious work connected with such a project

Footprinting of Infants—The public health committee studied the problem of permanent identification of the newborn child With the aid of the F B I and the New York City Police Department it drew up a resolution suggesting that the sanitary code of New York City be amended to require that all hospitals and institutions giving lying-in and neonatal care take footprints of the infant and fingerprints of the mother One set is to be a permanent record on the infant's chart This resolution was passed by the board of health and has since become part of the New York City Health Code

Directory of Medical and Social Services—The public health committee is, at present working on a directory of medical and social services for the practicing physician Originally, knowledge of these services was to be used as a basis for public health programming in the fields of mental health and geriatrics As facts were gathered, the committee broadened its scope to include all facilities which are concerned with the health of the community

When all material was organized and classified, it was found to be an excellent guide to the practicing physician in his quest for further service to the patient At the office or bedside of the patient, when problems arise that are not in the scope of medical diagnosis and treatment, the directory will be of great value in the search for community resources necessary to the patient

Special Investigations and Reports—The following investigations have been made and reports submitted to the Medical Society of the County of Kings by the Public Health Committee fluoridation of drinking water, revision of the sanitary code, private nursing homes, radioactive fallout, radiologic health hazards, deaths caused by side arm gas water heaters, case finding surveys of syphilis and diabetes, state and federal government control of poultry inspection, hospital epidemiologists, tetanus immunization program for allergic persons, industrial workers, and campers, program for the aged, and a chronic disease program

Summary

The public health committee of the Medical Society of the County of Kings is a cross section of the practicing physicians in Kings County

The previously mentioned programs were highlights of the committee's activities The focus of each program was on local needs of the community, and priority was given to those problems most pressing and requiring immediate attention This report demonstrates what can be done by dedicated men who unite for the common purpose of serving their community

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J A M A, July 30, 1960

BLOOD COUNTS AND LONG-TERM ANTIBIOTIC THERAPY

STUDIES ON DERMATOLOGICAL PATIENTS RECEIVING ANTIBIOTICS AND/OR SULFONAMIDES

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and
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The charts of 100 dermatological patients seen in private practice, who had received one or more antibiotic agents systematically for more than two months, were drawn at random from the authors' files and reviewed. Minor variations from what is considered normal in peripheral blood counts occurred in 54 of the patients. Leukocytosis was noted in 34, leukopenia in 7, and reversal of the polymorphonuclear leukocyte–lymphocyte ratio in 19. Other changes included eosinophilia, presence of atypical lymphocytes, and toxic granulations. Therapy of anemia was indicated in only one patient. The changes in this series may or may not be attributable to the antibiotics or sulfonamides; they were never dangerous, though patients should be made to understand that antibacterial agents should never be taken indiscriminately or without regular medical examination.

In our experience and that of others, some of the more recently developed systemically acting antibacterial agents have been among the most effective forms of therapy for certain dermatoses. However, in many instances of chronic or chronically recurrent dermatoses, the antibiotic or sulfonamide must be administered for months or even years. When patients take these agents by mouth for such prolonged periods the active phases of various dermatoses may be suppressed. Many publications on the dermatological uses of the various systemically acting antibacterial compounds may be found in the literature, but relatively few of them refer to long-term administration of these agents.[1] One of the strongest factors limiting the long-term oral administration of antibacterial agents is concern for the danger of damaging the hematopoietic tissues and producing blood dyscrasias. We have studied this aspect of the use of these agents in our dermatological practice, and our observations will be found in the following report.

Subjects and Procedures

The charts of 100 patients seen in private practice who had received one or more of the antibacterial agents for more than two months were drawn from our files at random and reviewed. (No particular selection of patients was attempted. The 100 patients included in this study represent but a fraction of the total number so treated by us.) The diseases treated are listed in table 1.

The dosage schedules were as follows: Broad-spectrum antibiotics were given in amounts of 250 mg four times daily for four days, then 250 mg three times daily for three days, and then 250 mg twice daily. Penicillin was given in amounts of 200,000 to 400,000 units (or equivalent) orally three to four times daily. Sulfonamides were given in amounts of 0.5 to 1.0 Gm. two to four times daily. After this initial schedule, the daily dose of each of these drugs was gradually decreased or increased, depending on the course of the disease. The details of the administration of these drugs and their side-effects have already been published in appropriate articles on the subject.[2]

Among the 100 patients treated there were twice as many women as men, probably because most of the randomly selected cases were acne vulgaris, for which women seek help more often than men. The age range was from 12 to 60 years, most patients being between 15 and 29 years old.

The various antibiotics used and the frequency with which they were prescribed (some patients received more than one antibiotic, taking a course of one followed by a course of one other or more) are listed in table 2. While the maintenance dose sufficing to suppress the manifestations of their dermatoses (morbidostatic dose) was sometimes as low as 125 mg. of a broad-spectrum antibiotic every third day, most patients were taking 250 to 500 mg. daily at the time the compilation was made. Forty-one patients took one or more of the antibacterial agents for about three months (occasionally less), 24 took them for one year or more, and the remaining 35 took them for periods varying between three months and one year.

Complete blood counts generally were made every two weeks during the initial months of therapy and less often thereafter. Ordinarily, blood was taken at about the same time of day, although we did not record when the counts were taken in relation to ingestion of food. No matter how small the dose of antibiotics taken, counts were requested at least every two months.

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Results

No alterations beyond the limits of normal occurred in the peripheral blood counts of 46 patients Tables 3 and 4 summarize the changes that occurred, the time of onset of these changes, the antibiotic involved, and certain details concerning the dosage Changes occurred in 54 patients When more than one type of change took place in the counts of any one patient, each was recorded separately, thus accounting for the 70 entries under 'No of Patients" in tables 3 and 4

Table 1 —*One Hundred Randomly Selected Patients with Dermatoses Given Long-term Antibiotic and/or Sulfonamide Therapy*

	Patients No
Acne vulgaris (usually severe or recalcitrant)	81
Acne varioliformis	1
Atopic dermatitis (impetiginized)	1
Dermatitis factitia	1
Dermatitis repens	1
Ecthyma	1
Folliculitis	2
Furunculosis	1
Hidradenitis suppurativa	2
Onychomycosis (with paronychias)	1
Otitis externa	3
Pili incarnati	1
Pseudo folliculitis	1
Rosacea	2
Subacute lupus erythematosus	1

Leukocytosis —As noted in table 3, leukocytosis (more than 10,000 white blood cells per cubic millimeter) occurred in 34 patients The average count of white blood cells was 11,800 and the highest, 17,600 per cubic millimeter The time elapsed after starting therapy with the antibacterial agent and before this change was noticed varied from one week to 15 months Of the 34 patients, 24 exhibited leukocytosis within the first two months after initiation of therapy A few patients demonstrated leukocytosis on several occasions There were times when the inflammation or infection accompanying the eruption could be incriminated as contributing to the increase in the number of white blood cells However, this change appeared to be unrelated to the degree of tissue inflammation in most instances, since the leukocytosis was not noted at the time of the first count when the tissue involvement and inflammation were at their highest Furthermore, many patients presenting the same or greater amounts of inflammation of their skin failed to show any abnormalities in their blood count

Table 2 —*Long-term Antibiotic and/or Sulfonamide Therapy in 100 Patients with Dermatoses*

	Drug Prescription No
Chloramphenicol (Chloromycetin)	8
Chlortetracycline (Aureomycin) hydrochloride	2
Erythromycin (Ilotycin)	1
Novobiocin (Albamycin) sodium	1
Oleandomycin and tetracycline (Signemycin)	1
Oleandomycin and tetracycline (phosphate buffered) (Signemycin V)	1
Oxytetracycline (Terramycin)	2
Phenoxymethyl penicillin (Pen Vee)	2
Potassium penicillin G plus sulfisoxazole (Gantricillin)	1
Potassium penicillin C (orally given) (Pentids)	11
Sulfisoxazole (Gantrisin)	4
Tetracycline (Achromycin or Polycycline) hydrochloride	21
Tetracycline hydrochloride buffered with sodium meta phosphate (Achromycin V)	2
Tetracycline hydrochloride plus nystatin (Mysteclin)	31
Tetracycline phosphate complex plus nystatin (Mysteclin V)	6
Tetracycline phosphate complex plus nystatin (Comycin)	64

Leukopenia —Leukopenia occurred in seven patients, the average count in these instances being 4,500 white blood cells per cubic millimeter Four patients showed this alteration within the first two months of therapy, in one it did not occur until the third year

A reversal of the ratio between the number of polymorphonuclear leukocytes and lymphocytes was demonstrated in 19 patients (the average lymphocytosis was 52%) In five additional cases the number of these two types of cells was equal Here again the change occurred early in many of the cases Fifteen patients showed the alteration within the first two months, although one patient took antibiotics for two and one-half years before the reversal was noted

Table 3 —*Type of Change in Peripheral Blood Count* in 100 Dermatological Patients Receiving Long-term Antibiotic or Sulfonamide Therapy*

	No of Patients	Average Time of Onset of Change After Initiation of Therapy Mo †
Leukocytosis	34	2(24)
Leukopenia	7	2(4)
Reversal of polymorphonuclear leukocyte-lymphocyte ratio	19	2(15)
Atypical lymphocytes	2	9(1)
Toxic granulation	2	2(both)
Eosinophilia	6	3½(3)

*Figures for normal blood count taken from Wintrobe Clinical Hematology ed 3 1951 Philadelphia Lea & Febiger p 95 (table V) and p 206 (table VIII) white cell count 5 000 to 10 000/cu mm red cell count male 5 4± 0 8 x 10^6/cu mm female 4 8± 0 6 x 10^6/cu mm hemoglobin level males 16± 2 0 Gm % females 14± 2 0 Gm % neutrophils mature 54-62% band forms 3-5% eosinophils 1 3% (5%) (an eosinophil count of 4 to 5% occurring on but one or two widely separated counts appeared with such frequency that 5% was considered the upper limit of normal for this study) basophils 0 1% lymphocytes 25-33% and monocytes 3 7%

†Figures in parentheses indicate number of case

Other Changes —Other changes, such as eosinophilia, the presence of atypical lymphocytes, and toxic granulation are summarized in table 3 Several patients showed sporadic increases in the number of eosinophils and, at times, monocytes Although an increase or decrease in the amount of hemoglobin and the number of red blood cells was noted occasionally, therapy for the anemia was indicated in only one patient

Analysis of Changes in Blood Count —The presence of these variations from what is considered a normal blood count does not mean that they are necessarily the result of the long-term systemic antibacterial therapy It would have been desirable to have a corresponding control group of patients not receiving systemic antibacterial therapy To our knowledge, repeated blood counts have not been taken as a routine procedure, in instances of any of the diseases listed, to ascertain what changes and fluctuations might take place spontaneously Most important is the fact that no changes of serious consequence were noted in the peripheral blood picture of any patient treated with systemically acting antibacterial agents over prolonged periods (This finding confirms our own and our colleagues' observations on thousands of other dermatological patients who have received antibiotics orally for prolonged periods without a single case of severe or serious blood changes, with the possible exception of those taking chloramphenicol [Chloromycetin]) Furthermore, any variations from the normal which did occur reverted to normal in spite of continued administration of the drug or by simply discontinuing its use temporarily There was no evidence that the observed minor changes in the blood count occurred in certain diseases rather than others (see table 5 and compare with incidence of diseases treated [table 1])

TABLE 4 —*Change in Peripheral Blood Count in 100 Dermatological Patients Given Long-term Antibiotic and/or Sulfonamide Therapy*

No of Patients Taking Drug	Blood Change		Status of Drug Therapy at Time of Observation		
	Type*	No of Patients	Total Time Taken	Daily Dose	Length of Time Daily Dose Taken
Tetracycline hydrochloride plus nystatin (Mysteclin) 31	Leukocytosis	7	2 3 mo	250-500 mg	2 wk in most cases
	Reversal of P/L ratio	6	1½ mo	250 500 mg	3 cases within 1 mo
	Eosinophilia	6	1 wk to 11 mo	500 750 mg	1 wk in most cases
	Atypical lymphocytes	1	*9 mo*	500 mg	2 wk
Tetracycline phosphate complex plus nystatin (Comycin), 64	Leukocytosis	11	1½ mo	250-500 mg	1 mo or less
	Leukopenia	4	2 mo	500 mg	3 cases within 3 wk
	Reversal of P/L ratio	6	1 mo or less	500 mg	All cases within 3 wk
	Eosinophilia	1	3½ mo	500 mg	1 mo
	Toxic granulation	1	1 mo	500 mg	2 wk
Tetracycline (Achromycin) hydrochloride 19	Leukocytosis	9	3 cases within 1 mo	250 500 mg	4 cases within 2 wk
	Leukopenia	3	1 3 yr	250 mg	2 cases within 9 mo
	Reversal of P/L ratio	4	1 mo to 1⅔ yr	500 mg	1 case within 3 mo
	Atypical lymphocytes	1	2½ yr	500 mg	2 mo
	Toxic granulation	1	2 mo	750 mg	1 mo
Tetracycline phosphate complex plus nystatin (Mysteclin V) 6	Leukocytosis	1	2 mo	750 mg	3 wk
Chloramphenicol (Chloromycetin) 8	Leukocytosis	2	2 wk	500 mg	2 wk
	Reversal of P/L ratio	1	1 wk	1000 mg	1 wk
Sulfisoxazole (Gantrisin), 4	Leukocytosis	2	1 mo	2 Gm	1 mo
Potassium penicillin G (Pentids) 11	Leukocytosis	2	2 wk	1 200 000 units	2 wk
	Reversal of P/L ratio	1	2 mo	400 000 units	1 wk
Phenoxymethyl penicillin (Pen Vee) 2	Reversal of P/L ratio	1	2 wk	750 mg	1½ wk

* P/L ratio=ratio of polymorphonuclear leukocytes to lymphocytes

The duration of these changes was studied whenever possible In several instances this could not be accomplished because the patient failed to return for follow-up visits However, in 18 patients the leukocytosis lasted one month or less, in 5 patients two months, and in 1 patient over five months In five patients the leukopenia persisted two months or less In 11 patients the reversal of the polymorphonuclear leukocyte–lymphocyte ratio lasted two months or less None of the other alterations persisted for more than two months

Comments

In this study 100 patients presenting a wide variety of dermatoses were continuously treated with systemically acting antibacterial agents for a period ranging from months to many years Routine blood counts were performed on all these patients

Minor variations from what is considered a normal blood count were noted in 54 of these patients Most of the abnormalities reverted to normal while the patient was still taking the antibiotic or when its administration was discontinued One patient, however, had a persistent leukocytosis four months after the cessation of antibiotic therapy, but he also had a fever of unknown origin Four patients had a leukocytosis at their last count but never returned for a follow-up visit (Three of them had several such increases) The same situation obtained for three patients who had a reversal of the polymorphonuclear leukocyte–lymphocyte ratio (One patient had several such bouts)

This study indicates that changes in the peripheral blood count do occur during the long-term administration of antibiotics These changes may or may not be attributable to the drugs In our series they were never dangerous but in general only temporary and, ordinarily, did not necessitate the cessation of therapy When a count appeared grossly abnormal and a repeat count performed within five days again showed the same abnormality, use of the antibacterial agent was discontinued If a change in the count appeared during therapy with chloramphenicol, this medication was discontinued immediately because of the previous reports of serious end-results[3]

Summary and Conclusions

The charts of 100 otherwise unselected and randomly chosen private patients with dermatoses who had received orally one or more antibiotic agents, sulfonamide drugs, or both for more than two months were reviewed with respect to changes in the peripheral blood count Complete blood counts generally were performed every two weeks during the initial months of therapy and somewhat less often thereafter

During therapy, leukocytosis occurred in 34 patients, leukopenia in 7, and a reversal of the polymorphonuclear leukocyte–lymphocyte ratio in 19 patients Atypical lymphocytes were seen in two cases, "toxic" granulation in two, and eosinophilia above 5% in six While serious side-effects have been reported following the use of sulfisoxazole and chloramphenicol, we did not encounter such reactions

TABLE 5 –*Incidence of Blood Changes in Patients with Dermatoses on Long-term Antibiotic and/or Sulfonamide Therapy*

	Blood Change	
	Type*	No of Cases
Acne vulgaris	Leukocytosis	26
	Leukopenia	7
	Reversal of P/L ratio	17
	Atypical lymphocytes	2
	Toxic granulation	2
	Eosinophilia	6
Otitis externa	Leukocytosis	1
Folliculitis of beard	Leukocytosis	1
Subacute lupus erythematosus	Leukocytosis	1
Ecthyma	Leukocytosis	1
Dermatitis repens	Leukocytosis	1
Atopic dermatitis	Eosinophilia	1 (present originally)
Rosacea	Leukocytosis	1
	Reversal of P/L ratio	1
Furunculosis	Leukocytosis	1
Folliculitis	Leukocytosis	1
Dermatitis factitia	Reversal of P/L ratio	1

P/L ratio=ratio of polymorphonuclear leukocytes to lymphocytes

Of the 93 patients whose course was followed up and who returned for final examination, only 1 showed a persistent change, a leukocytosis This patient, however, had a fever of unknown origin Four patients who did not return for final examination had a leukocytosis at their last peripheral blood count and three had a reversal of the polymorphonuclear leukocyte–lymphocyte ratio No serious or dangerous changes in hematopoiesis occurred, and persistent minor changes in the peripheral blood count occurred only rarely as a result of long-term antibacterial therapy

All patients should be made to understand that antibacterial agents must never be taken indiscriminately or without regular medical examinations Complete blood counts need not, however, be taken more than once a month, particularly when the patient has been on oral antibacterial therapy and is taking smaller doses e g, 250 mg or less of an antibiotic per day

Although our conclusions are based on patients having dermatological diseases (preponderantly acne vulgaris), we believe that they can probably be applied to patients affected with other conditions for which systemically acting antibacterial agents may have to be used for long periods

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The blood counts for this study were performed by Mrs Alexandra Dominick our office technician except for a few which were performed by licensed laboratories

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GYNECOMASTIA ASSOCIATED WITH LUNG CANCER

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Gynecomastia occurring in three men aged 44, 51, and 60 years was found to be associated with bronchogenic carcinoma In the first patient the primary complaint was painful swelling of the knees, and the gynecomastia was noted two years later when the patient was hospitalized In the second patient the gynecomastia was the initial symptom It developed in the third patient weeks after thoracotomy at which an unresectable carcinoma of the lung had been found Assessment of the patients' endocrine status, including determinations of 24-hour excretion of estrogens and of 17-ketosteroids, failed to identify any one endocrine factor that would explain the gynecomastia in all patients

During recent years numerous instances of systemic manifestations of "nonendocrine" tumors have been observed and recorded Lung cancer particularly has been identified with the capacity to produce bone and joint lesions, hypercalcemia, and peripheral edema However, the occurrence of gynecomastia in association with bronchogenic carcinoma has apparently escaped general attention I have found only one brief case report in the English-language literature, published by Altschul in 1938,[1] although a number of cases have been recorded in foreign language journals, chiefly from Latin America but also from France and Belgium[2] The present report is presented with a view to effecting a more general awareness that gynecomastia is at times associated with lung carcinoma and may occasionally be the initial physical manifestation of this neoplasm

Report of Cases

CASE 1 —Case 1 is an example of bronchogenic carcinoma associated with gynecomastia, generalized joint disease, hypertrophic pulmonary osteoarthropathy, and peripheral edema A 44-year-old man was admitted to the University Hospital on Sept 25, 1957, with the complaint of painful swelling of his knees for the past two years, which had progressed to such a degree that he could hardly walk Early in 1957 he had developed dyspnea associated with pain in the chest and left arm, both of which came on during exertion and were essentially absent during rest Edema of the ankles and feet had been present for several months He had also noted that the ends of his fingers had become larger (clubbing) A productive cough had developed three weeks prior to admission

Physical examination revealed bilateral gynecomastia of moderate degree (fig 1), swollen and tender knee joints, and 4+ pitting edema of the ankles and feet The blood pressure was 170/100 mm Hg He also had limitation of arm movement because of pain in each shoulder, and there was definite clubbing of the fingers

The opinions of physicians at this point centered around arthritis, as it was the primary problem Attention was directed to excluding rheumatoid arthritis, a collagen disease such as lupus erythematosus, or an infectious agent such as the gonococcus from the differential diagnosis Periarteritis nodosa was also considered Moreover, since on admission urinalysis had shown 4+ sugar, diabetes mellitus was considered to exist and was controlled by dietary means without insulin

Laboratory data were as follows hematocrit reading 44% and hemoglobin level 14 2 Gm %, white blood cell count 6,000 per cubic millimeter, with an essentially normal differential count, and a platelet count of 331,000 per cubic millimeter Urinalysis revealed 4+ sugar but no acetone The fasting blood sugar level was 135 and 150 mg % on separate occasions, a postprandial level determined two hours after a meal was 325 mg % The nonprotein nitrogen level was 23 mg %, serum phosphorus level 3 2 mg %, alkaline phosphatase level 3 9 Bodansky units, and total serum protein 5 9 Gm %, with 3 3 Gm % albumin and 2 6 Gm % globulin The urinary 17-ketosteroid excretion was 9 9 mg in 24 hours and the sulfobromophthalein retention 5% The test for lupus erythematosus gave a negative result, as did the serologic test for syphilis Sputum studies for acid-fast organisms and fungi gave negative results Fluid aspirated from a knee joint revealed no micro-organisms on smear or culture, and its protein concentration was 2 8 Gm %

The roentgenographic studies were of particular interest The chest x-ray revealed a mass along the upper border of the right hilum which was judged to represent a neoplasm The bones of the hands, forearms, and lower leg and knee regions showed pulmonary osteoarthropathy In fact, changes in the long bones were so marked that the films were placed in the teaching file

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At bronchoscopy no lesion was visualized in the tracheobronchial tree, but bronchial washings contained malignant tumor cells. Biopsy of a specimen from the scalene fat pad showed no tumor metastasis. At the time of thoracotomy, on Oct. 23, 1957, a right pneumonectomy was performed for what appeared grossly to represent a carcinoma of the right upper lobe, adjacent to the hilum. The pathologist reported an infiltrating, anaplastic, epidermoid carcinoma of the lung arising in the region of the right apical bronchus. None of the lymph nodes submitted with the lung specimen contained metastases.

The patient's postoperative course was uneventful and he was discharged from the hospital on Oct. 31, 1957. At this time the edema of the legs had disappeared and the joint pain had largely subsided. The gynecomastia appeared to have diminished somewhat, and the breasts were less firm and tender than they had been preoperatively. He did not keep his follow-up appointments until Feb. 4, 1958, about three months after operation. At this time he was able to walk an unlimited distance without dyspnea and the cough present preoperatively was absent. Ankle and pedal edema were absent, there had been no joint pain or stiffness since discharge, and he had observed that the ends of his fingers had diminished in size. The breasts were still slightly enlarged, but they were soft and no longer tender to palpation. The chest x-ray showed the findings usual after a pneumonectomy, the right hemithorax being completely opaque except at the apex where there appeared to be a slight residual amount of air. There was considerable change in the appearance of the periosteal new bone formation in the right forearm which had been noted preoperatively. The new bone now appeared more uniform and compact than at the time of the studies made before the surgical removal of the lung tumor. Similar changes were noted in the upper portion of the right femur, the left humerus, and other bones. Unfortunately, the patient's subsequent course was one of progressive deterioration, and he died at home on May 4, 1958.

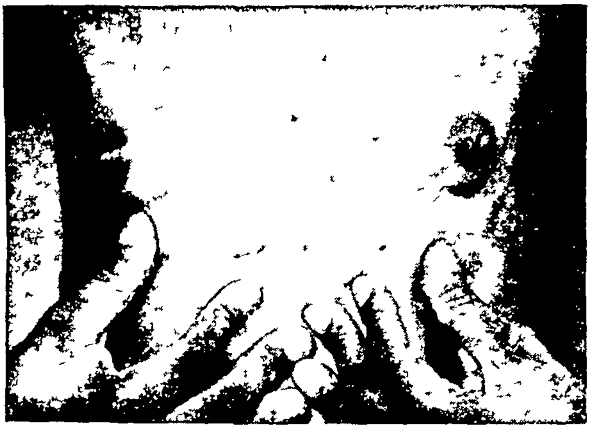

Fig. 1 (case 1).—Patient with gynecomastia. Bone and joint changes secondary to bronchogenic carcinoma developed months prior to appearance of gynecomastia in this 44-year old man.

Comment.—This unusual case illustrates especially well the complex findings which may be associated with lung cancer. The patient was admitted for the study of arthritis and a mild diabetes mellitus. The bone and joint changes, with associated pitting edema, proved to be secondary to a right pulmonary malignancy. The diabetes was apparently incidental.

The gynecomastia diminished somewhat after right pneumonectomy, but it did not disappear entirely. This patient had lost about 25 lb. (11 kg.) during his illness, and his testes were recorded as being small. The liver would not appear to have been seriously involved with malignancy, since it was not palpable and since the sulfobromophthalein retention was 5%. It is possible that testicular atrophy, secondary to malnutrition and chronic disease, may have permitted the hormonal imbalance which produced gynecomastia in this man, but the level of urinary 17-ketosteroid excretion (9.9 mg. in 24 hours) was well within normal limits.

Case 2.—Case 2 is an example of gynecomastia as an initial symptom in lung cancer. A 51-year-old man was in his usual state of health until March, 1957, when he began to notice tenderness of his nipples. This condition gradually progressed to involve the breasts proper, which became enlarged but without nipple discharge. He consulted an osteopath in Texas and was given 'hormones' which he took for several weeks without avail, breast enlargement persisted. By June, 1957, he had begun to have aching pain in the lower part of his chest on the left side, which occurred at first only at night but later was present most of the time. He began to require treatment with codeine for this pain, but he had had no fever, chills, night sweats or weight loss during the entire period. Three weeks prior to admission to the University Hospital on July 15, 1957, he had developed a fairly severe cough which was productive of a white frothy sputum, and during the last few days he had begun to cough up bright red blood. A roentgenogram of the chest taken about one month earlier was said to have shown a thickening of the left lower lobe.

Physical examination revealed bilateral gynecomastia (fig. 2), evidence of disease in the left lung and atrophy of the testes. There was no clubbing of the fingers. Laboratory findings on the blood and urine were essentially normal: total serum protein content 6.7 Gm.% with 3.8 Gm.% albumin and 2.9 Gm.% globulin, serum phosphorus level 3.1 mg.%, with an alkaline phosphatase level of 3.0 units, nonprotein nitrogen level 25 mg.%, and sulfobromophthalein retention 7%. The 24-hour urinary excretion of 17-ketosteroids was 5 2 mg, a subnormal value for a 50-year-old man and in accord with the bilateral testicular atrophy that had been noted on the physical examination The plasma estrogen level was considered to be within normal limits, but the 24-hour urinary excretion of estrogens was reported as "increased" Sputum studies were negative for acid-fast organisms and fungi

The chest x-ray revealed a cavitary lesion involving both the left upper and left lower lobes, situated laterally At bronchoscopy the tracheobronchial tree appeared to be within normal limits and bronchial washings were negative for tumor cells Thoracotomy was performed on July 15, 1957, and the "abscess cavity was found to involve the lateral portions of the left upper and lower lobes with apparent invasion of the pleura and intercostal muscles of the adjacent thoracic wall On frozen section examination the walls of the locally excised cavity appeared to suggest possible fungus disease, but subsequent paraffin sections available postoperatively revealed carcinoma Although at operation the possibility of tumor had been considered a likely one, the invasion of the chest wall rendered extensive resection inadvisable The patient recovered uneventfully from the operation and received cobalt radiation therapy However, his condition gradually became worse and he died after pulmonary hemorrhage on Nov 28, 1957

At autopsy the following pertinent findings were recorded An extensive tumor was present in the left lung, associated with hemorrhage The liver weighed 2,100 Gm and, although it contained scattered tumor nodules, was by no means extensively involved The two adrenal glands together weighed a total of 20 Gm, both glands were normal in appearance, and there was no evidence of involvement by tumor metastasis The breasts exhibited gynecomastia, manifested by a great proliferation of the ductal system Surrounding these proliferating ducts was an area of loose connective tissue which was moderately cellular Between these areas of proliferating ducts with their adjacent connective tissue there was a second type of dense hyalinized connective tissue which was relatively acellular

CASE 3—Case 3 is an example of gynecomastia developing weeks after thoracotomy at which an unresectable carcinoma of the lung had been biopsied A 60-year-old man returned to the emergency room requesting treatment with narcotics for pain about eight weeks after a thoracotomy at which an unresectable bronchogenic carcinoma had been biopsied He exhibited moderate bilateral tender gynecomastia Inasmuch as I had operated on the patient myself and was familiar with his condition, he was not readmitted for further studies and no photograph was taken

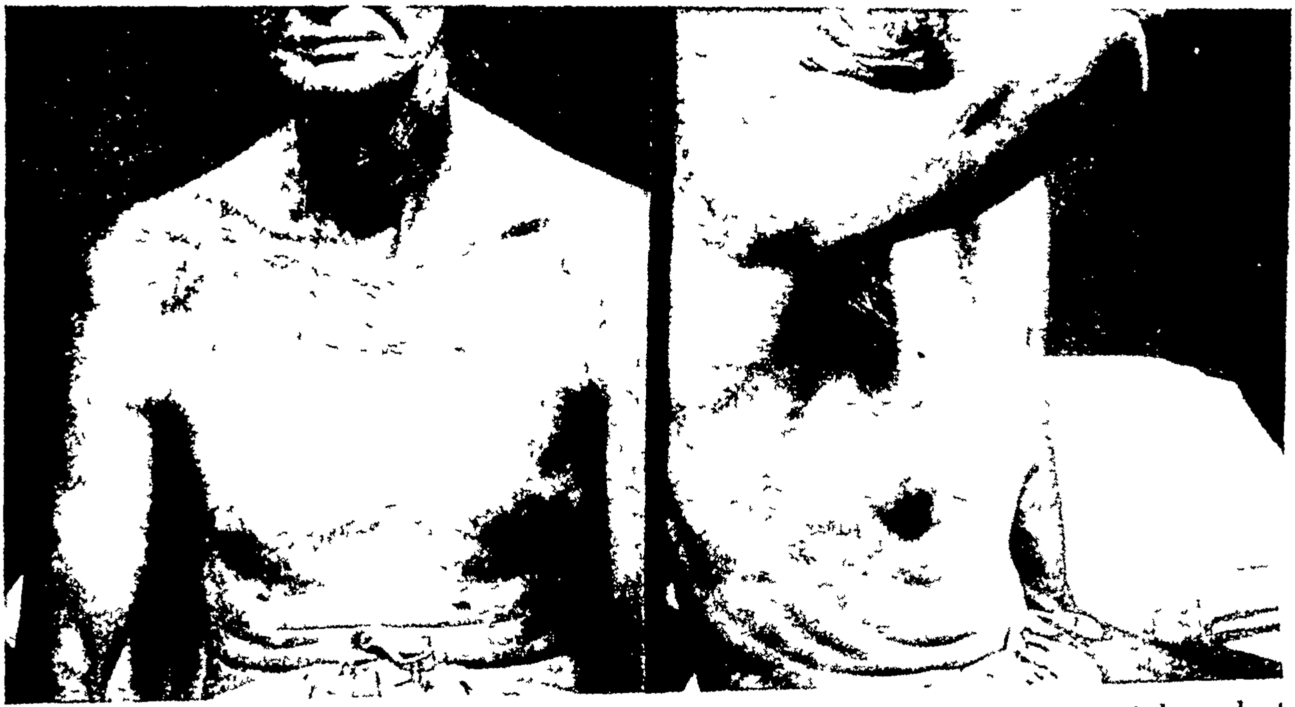

Fig 2 (case 2)—Patient with gynecomastia and bronchogenic carcinoma Gynecomastia was initial complaint in this 51-year-old man

Comment

Hypertrophy of the breasts in men is usually met under one or a combination of the following circumstances 1 At puberty here the dominance of androgen secretion has not yet become established over the adrenal estrogens Moreover, it is possible that the testes themselves secrete substances of an estrogenic nature which can cause gynecomastia in young boys, for this temporary gynecomastia is associated with other evidence of beginning puberal development There would seem to be no reason why the adrenal estrogen secretion should increase at this time Such temporary gynecomastia at puberty, either unilateral or bilateral, usually disappears in a few months It is reported to occur in possibly one-third of all boys, at least to a degree, although I have not observed it with such frequency 2 Estrogen-secreting adrenal tumors such tumors are rare, but they do occur Perhaps less than 30 have been reported in the literature 3 Estrogen therapy in male patients marked gynecomastia may accompany the use of estrogen therapy for prostatic cancer or as prophylaxis against further attacks of coronary occlusion

4 Liver disease patients with cirrhosis of the liver frequently manifest gynecomastia It has been hypothesized that, first, the cirrhotic liver is more effective in deactivating androgens than it is in deactivating estrogens Second, such patients frequently have a degree of testicular atrophy, associated with a diminished excretion of 17-ketosteroids, reflecting a reduction in androgen secretion Thus, if the adrenals continued to secrete estrogens at even a normal rate and the production of androgens by the testes is diminished—particularly in the possible presence of an increased capacity of the liver to inactivate the androgens in contrast to the estrogens—gynecomastia might be produced 5 Starvation gynecomastia was observed in some American men released from prisoner-of-war camps after World War II Most of them had been subjected to at least qualitative malnutrition They often exhibited a degree of testicular atrophy, and it was suspected that certain subtle changes in liver function had also occurred

6 Chorioepithelioma in men a chorioepithelioma may arise in the testes, mediastinum, or adjacent to the pineal gland It has been suggested that these totipotential cells may secrete estrogens in addition to other hormonal substances 7 Other endocrine disorders of the pituitary and gonads, 8 essential gynecomastia in a patient in whom no probable etiological explanation is apparent, 9 certain lesions involving the spinal cord and nerves, and 10 lung cancer (and other chronic pulmonary disease)

The cause of the gynecomastia associated with bronchogenic carcinoma reported herein is not entirely clear However, all observers agreed that two of the three patients, in whom the testes were carefully examined, showed a considerable degree of testicular atrophy In one patient the 24-hour level of excretion of 17-ketosteroids was subnormal, but in another the level was within normal limits, such studies were not made in the third subject The urinary excretion of estrogens, measured in only one patient, was reported as increased In the one patient on whom an autopsy was performed the liver was found to contain a few metastases, but these were not extensive The adrenal glands were considered to be within normal limits One patient had lost considerable weight, and a certain degree of chronic malnutrition might have been present In contrast, one patient had lost virtually no weight and did not appear to be malnourished at the time of his first admission

It is possible that the gynecomastia encountered in these patients was secondary to chronic disease with testicular atrophy Nevertheless, the possibility of the secretion of an estrogen-like factor by the pulmonary tumor cannot be entirely discounted This alternative is rendered even more intriguing by recent reports which indicate the capacity of various "nonendocrine" tumors to produce 'endocrine" or systemic changes

Summary and Conclusions

Three cases of gynecomastia occurred in association with bronchogenic carcinoma In one patient gynecomastia was the presenting complaint and was treated with hormones for several weeks before chest pain led to a search for intrathoracic disease and disclosure of the lung lesion Breast enlargement appears to be associated with bronchogenic carcinoma more frequently than with many other tumors The endocrine factors responsible for the bilateral gynecomastia are not clear Some degree of testicular atrophy was observed in all three patients, and a subnormal level of androgen excretion was reflected in the 24-hour 17-ketosteroid excretion (5 3 mg) recorded in one of two patients so studied, in this same subject the 24-hour urinary excretion of estrogens was reported as increased Gynecomastia is only one of numerous systemic manifestations which have now been reported in association with various localized 'nonendocrine" tumors

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ACTIVATION OF PEPTIC ULCER BY NICOTINIC ACID

REPORT OF FIVE CASES

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Side reactions encountered when patients take substantial doses (3.0 to 7.5 Gm.) of nicotinic acid per day are exemplified in the histories of five patients who were being treated for hypercholesteremia. In addition to the underlying vascular disease present in every case, two patients were known to have had peptic ulcers before, two had had other upper gastrointestinal symptoms, and one showed signs of previous duodenal ulceration. After prolonged administration (up to 124 weeks in one case) of nicotinic acid, all developed symptoms and signs of active ulcers. When the nicotinic acid was administered in the form of tablets containing a buffer the gastrointestinal difficulties subsided promptly. The use of buffered preparations of nicotinic acid is suggested when long-term administration is necessary.

Since 1955, studies by various investigators have demonstrated that nicotinic acid in large doses can reduce elevated serum cholesterol levels in many persons. Despite repeated warnings that this treatment is still considered experimental,[1] there is no doubt that many physicians are using this method of therapy in selected patients. For this reason, it is the responsibility of investigators observing a large series of patients to report adverse effects of this form of medicament as soon as definite information becomes available. It is the purpose of this communication to report activation of peptic ulcer by administration of nicotinic acid to five patients, and to consider methods of eliminating this hazard.

Nausea and vomiting were mentioned as possible side-effects of nicotinic acid therapy in the preliminary report on the first long-term study in human beings.[2] Later reports indicated that although these side-effects were infrequent, they did cause sufficient discomfort in a few patients to require cessation of therapy.[3] Belle and Halpern[4] reported gastrointestinal distress in about 40% of their 48 patients, but did not specify the exact symptoms. They also reported reactivation of symptoms of peptic ulceration in two patients.[4] Altschul and Hoffer[5] suggested that high acidity rather than the specific action of plain nicotinic acid might account for the occasional gastrointestinal reactions. They advised the administration of a buffered solution of nicotinic acid, with use of sodium bicarbonate alone or with potassium bicarbonate as the buffering agent.

Since May, 1956, 90 patients have participated in the Jackson Clinic and Foundation study of the use of nicotinic acid for hypercholesteremia. About 50 persons are currently in the study program. Twenty-nine patients have been studied for more than two years and 19 others studied for more than one year. Details of materials and methods have been reported previously, along with a summary of the results.[3a] Within the past year, the third year of the study, five patients taking large doses of nicotinic acid have shown evidence of activation of peptic ulcers, with occult bleeding in one.

Report of Cases

CASE 1.—A 58-year-old man was discovered to have hypercholesteremia in 1956 and began taking nicotinic acid in January, 1957. He had had two myocardial infarctions (1948 and 1954). In 1949 roentgenograms had been made of the upper portion of the gastrointestinal tract because of excessive belching. Changes suggesting a duodenal ulcer had been found. He had been treated with an antispasmodic-sedative combination, but he had not followed a special diet or taken antacid. In 1955 he had experienced epigastric pressure of brief duration. Roentgenograms made at that time had shown an irritable, deformed duodenum, consistent with a diagnosis of duodenal ulcer. No diet or treatment program for peptic ulcer was being followed at the time that nicotinic acid therapy was started.

Average levels of serum cholesterol, beta-lipoprotein cholesterol, and the beta alpha$_1$-lipoprotein cholesterol ratio are given in table 1.

In January, 1959 (after 101 weeks in the study), the patient experienced nausea and vomiting for two or three days, accompanied by fever and chills, a condition which was diagnosed as gastroenteritis, probably of viral origin. After this episode he had dull epigastric pain at times. He stopped taking nicotinic acid and felt well. After one week he resumed nicotinic acid therapy and the epigastric pain recurred six days later. The discomfort persisted and was relieved by taking a proprietary antacid. His appetite was poor. He stated that this distress was similar to that he had had in 1955. Physical examination at that time (1959) gave negative results. Roentgenograms were not made again

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He was treated with milk between meals and an antispasmodic drug Nicotinic acid was given in the same dosage, but a buffered preparation was substituted The patient had no further symptoms, in fact he was able to take 7 5 Gm daily, a dosage which had earlier been found to provide the lowest serum cholesterol levels, smaller doses having failed to achieve normal levels

Case 2—A 38-year-old man was first seen at the Jackson Clinic in August, 1958, with a three-year history of claudication in both calves extending into the thighs and buttocks Physical examination and aortography resulted in a diagnosis of occlusion of the lower abdominal aorta Surgical exploration was performed, with bilateral lumbar sympathectomy and endarterectomy of the lower abdominal aorta and iliac arteries

After discovering that he had hypercholesteremia, therapy with nicotinic acid was begun in October, 1958 (see table 2)

Table 1—*Average Levels of Serum Cholesterol Beta-Lipoprotein Cholesterol, and Beta Alpha₁-Lipoprotein Cholesterol Ratio of Patient in Case 1*

Treatment Period Wk	Drug Given	Daily Dose Gm	Serum Cholesterol Level Mg per 100 Ml	Beta lipoprotein Cholesterol Level Mg per 100 Ml	Beta alpha₁ Ratio
Pretreatment	None		280		
0-12	Nicotinic acid	3	239		
12 30	Nicotinic acid	4 5-7 5	240		
30-42	Nicotinamide	7 5	318	230	6 1
42 56	Nicotinic acid	7 5	286	175	3 0
56-60	None		323	244	6 0
60 101	Nicotinic acid	6	244	189	3 7
107 135	Nicotinic acid buffered	7 5	239	176	3 5

The patient had had a duodenal ulcer in the past In 1942 a perforation had been repaired surgically and in 1943 a gastroenterostomy had been performed Subsequently recurrent ulcer symptoms had been treated by temporary dietary restriction, but he had not been following an ulcer regimen at that time

During a period of hospitalization for secondary infection of necrotic muscle of the anterior tibial compartment of the right leg, the patient had mild exacerbation of ulcer symptoms and his hemoglobin level fell from 13 5 to 11 2 Gm per 100 ml He had been in the study for 16 weeks, taking 3 Gm of nicotinic acid daily Results of guaiac tests for occult blood in the stools were positive on several occasions Treatment consisting of a liberal ulcer diet and antacid therapy was instituted A buffered nicotinic acid product was substituted for plain nicotinic acid The patient had no further gastrointestinal symptoms or evidence of bleeding

Case 3—A 40-year-old man was considered to be in good general health except that he was a vascular hyperreactor In February, 1956, he had had gaseous indigestion, attributed to dietary excess and increased consumption of alcohol at conventions Roentgenograms of the upper gastrointestinal area showed pylorospasm and irritable duodenal bulb but no deformity or crater No treatment was prescribed

After the presence of hypercholesteremia was discovered, the patient began to take nicotinic acid in August, 1957 (see table 3)

Table 2—*Averages of Blood Determinations Made in Various Periods of Treatment of Patient in Case 2*

Treatment Period Wk	Drug Given	Daily Dose Gm	Serum Cholesterol Level Mg per 100 Ml	Beta lipoprotein Cholesterol Level Mg per 100 Ml	Beta alpha₁ Ratio
Pretreatment	None		292	240	20 9
0-16	Nicotinic acid	3 0	260	204	3 1
16 44	Nicotinic acid buffered	3 0	269	161	2 4

In the summer of 1959 (after 96 weeks in the study) he began to experience nausea and vomiting, especially on Monday mornings He denied unusual diet or alcohol intake on the week-end No typical ulcer-like symptoms were described Roentgenograms revealed an irritable duodenal bulb with a deformity at the base consistent with a duodenal ulcer He was treated with an ulcer diet with anticholinergic and antacid medication The administration of a buffered nicotinic acid preparation was substituted for plain nicotinic acid, with prompt relief of gastrointestinal symptoms Several weeks later he had nausea without vomiting and decided to stop taking even the buffered preparation

Case 4—A 47-year-old man was first examined in June, 1957 Two months previously he had had transient numbness of the right hand and lip which had been called a stroke by his local physician The serum cholesterol level had been found to be 390 mg per 100 ml and a low-fat diet had been instituted During the next month he began to have substernal pain on effort, typical of angina pectoris During that month he lost weight from 173 to 161 lb (78 5 to 73 0 kg) His height was 66 5 in (166 25 cm) The serum cholesterol level was reported to be 290 mg per 100 ml at the end of the month Physical examination gave negative results The electrocardiogram made with the patient at rest was within normal limits and a standard two-step exercise test gave equivocal results The diagnosis of coronary atherosclerosis with angina pectoris

Table 3—*Averages of Blood Determinations in Various Periods of Treatment of Patient in Case 3*

Treatment Period Wk	Drug Given	Daily Dose Gm	Serum Cholesterol Level Mg per 100 Ml	Beta lipoprotein Cholesterol Level Mg per 100 Ml	Beta alpha₁ Ratio
Pretreatment	None		268	165	5 2
0-32	Nicotinic acid	3 0	200	136	2 8
32-44	Nicotinamide	3 0	201	183	4 7
44 56	Nicotinic acid	3 0	211	160	3 1
56-60	None		270	228	5 4
60-95	Nicotinic acid	3 0	173	125	2 5

and possible cerebral arterial insufficiency was made on the basis of the history

Blood tests during the period from June to August, 1957, gave the following average results serum cholesterol level 232 mg per 100 ml, beta-lipoprotein cholesterol level 169 mg per 100 ml, and beta alpha$_1$-lipoprotein cholesterol ratio 9 1 (see table 4)

In April, 1958, the patient experienced nausea and vomiting for about one week Physical examination and x-rays of the upper gastrointestinal tract gave negative results His weight at that time was 141 lb (64 kg) Treatment for several weeks with prochlorperazine relieved the nausea and vomiting The total amount given was about 300 mg

Early in 1959 he was found to have mild diabetes His weight was then 162 lb (73 5 kg) but fell to 140 lb (63 5 kg) on a 1,200 calorie diabetic diet In August, 1959, the patient complained of nausea which had been progressively worse for about two months He had vomited as many as four times daily for several days at a time, especially after meals, and had lost an additional 10 lb (4 5 kg) (to 130 lb [59 kg]) He was unable to eat much because he filled up quickly and became nauseated He had derived little or no benefit from taking prochlorperazine for a few weeks in July The total dose was again about 300 mg Roentgenograms of the gallbladder gave normal results, but upper gastrointestinal roentgenograms showed a small ulcer on the posterior wall of the duodenum Further questioning revealed that the patient had had similar symptoms intermittently for a 2-year period beginning 10 years previously No x-ray had been taken at that time, but symptomatic medicaments had been given

Treatment was begun with an ulcer diet, and antispasmodic, and antacid therapy Nicotinic acid was given in the same dosage (4 5 Gm daily), with use of a buffered preparation His symptoms were relieved almost immediately

Case 5 —A 42-year-old woman was first seen in December, 1956, because of the presence of hypercholesteremia which had been known to her for two and one-half years For 10 years the patient had experienced angina pectoris when shoveling snow or walking against a cold wind For a few months she had had claudication in both calves and posterior thighs when walking three or four blocks on the level She had xanthoma tendinosum on the extensor tendons of her fingers and on both Achilles tendons Her mother had died at 54 years of age of heart disease after several heart attacks Her father had died at 68 years of age of a stroke Two younger sisters had similar tendon deposits and xanthelasmata One brother had xanthelasmata Another brother had arcus senilis, as did the patient and her mother Several of the mother's siblings were known to have died of heart attacks at between 50 and 60 years of age, but none before the age of 50 years

She was not overweight A questionable small xanthelasma was present on the right lower eyelid Multiple small lesions of xanthoma tendinosum were present on the extensor tendons of the fingers of both hands and on both Achilles tendons Pulsations in the lower extremities were absent below the level of the femoral arteries

After several pretreatment blood tests, nicotinic acid therapy was started Despite the use of large doses for long periods, cholesterol levels were not reduced to the normal range

In December, 1957, one of the patient's brothers died at 46 years of age of a heart attack A paternal cousin with hypercholesteremia also had a heart attack at about the same time The patient experienced anxiety symptoms with hyperventilation during this period

Beginning in May, 1958, her dietary fat was restricted to 35 Gm daily in an effort to lower the cholesterol levels further Nicotinic acid therapy was continued as before at a dosage level of 7 5 Gm daily When no significant reduction occurred in serum lipid levels in the next nine months, a preparation of unsaturated fatty acids was added to the regimen, but no further reduction in cholesterol levels was observed

In March, 1959, the patient's sister died of a heart attack at 36 years of age Her serum cholesterol levels had been more than 600 mg per 100 ml The

Table 4 —*Averages of Blood Determinations Made in the Various Periods of Treatment of Patient in Case 4*

Treatment Period, Wk	Drug Given	Daily Dose Gm	Serum Cholesterol Level Mg per 100 Ml	Beta lipoprotein Cholesterol Level Mg per 100 Ml	Beta alpha$_1$ Ratio
Pretreatment	None		232	169	9 1
0-12	Nicotinic acid	3 0	226	170	5 6
12 34	Nicotinic acid	4 5	162	11[illegible]	5 [illegible]
34-46	Nicotinamide	4 5	29[illegible]	273	9 9
46 58	Nicotinic acid	4 5	180	157	6 3
58 62	None		241	176	6 7
62 10[illegible]	Nicotinic acid	4 5	153	131	3 8

Table 5 —*Averages of Blood Determinations Made in Various Periods of Treatment of Patient in Case 5*

Treatment Period Wk	Drug Given	Daily Dose, Gm	Serum Cholesterol Level Mg per 100 Ml	Beta lipoprotein Cholesterol Level Mg per 100 Ml	Beta alpha$_1$ Ratio
Pretreatment	None		430		
0-12	Nicotinic acid	3 0	278		
12 32	Nicotinic acid	4 5 to 7 5	283	216	4 7
32 44	Nicotinamide	7 5	446	308	6 9
44 62	Nicotinic acid	7 5	317	236	4 4
62 66	None		402	280	5 0
66 106	Nicotinic acid (35 Gm fat diet)	7 5	364	266	6 3
106 120	Nicotinic acid Linoleic acid (35 Gm fat diet)	7 5 3 13 [illegible]	371	255	5 8
120 124	None		414	280	6 9
124 138	Nicotinic acid	7 5	304	22[illegible]	[illegible]2

patient again experienced increased concern about her own condition. In August, 1959, she complained of morning nausea for about one month, with vomiting on four days in that period. She felt better when her stomach was full. Late in the evenings her symptoms were worse and were accompanied by heartburn, which was relieved by antacid therapy. Examination of the abdomen was unremarkable. Roentgenograms of the upper gastrointestinal area showed deformity of the duodenal bulb consistent with a duodenal ulcer. She was treated with an ulcer diet, anticholinergic drug and antacid therapy. Administration of a buffered nicotinic acid preparation was substituted for plain nicotinic acid. She felt well almost immediately and was able to continue her usual dosage of nicotinic acid without further symptoms.

Comment

Four of the five patients in whom peptic ulcers became active during nicotinic acid therapy had been in the study for long periods (99 to 124 weeks), with use of nicotinic acid in doses of 3.0 to 7.5 Gm. daily throughout most of that time. The other patient (case 2) had taken 3 Gm. of nicotinic acid daily for only 16 weeks when he showed evidence of occult bleeding from a previously known peptic ulcer, without any symptoms attributable to the ulcer.

Two patients (cases 1 and 2) were known to have had peptic ulcers previously but were not on any regimen of ulcer therapy until activation occurred during nicotinic acid treatment. Two other patients (cases 3 and 4) had previously had upper gastrointestinal symptoms resulting in roentgenologic study and symptomatic treatment when ulceration was not demonstrated by x-ray. In only one patient (case 5) was no previous history of either peptic ulcer or upper gastrointestinal symptoms elicited, but fluoroscopic demonstration of duodenal deformity suggested previous ulceration. The extreme worry of this patient regarding the deaths of several close relatives from complications of atherosclerosis was probably an important factor in development of peptic ulceration. Severe emotional stress was also present in other patients. One man (case 2) had aortoiliac vascular surgery for severe arteriosclerosis obliterans at 38 years of age, followed by necrosis and secondary infection of the anterior tibial musculature compartment in one leg, necessitating hospitalization and prolonged treatment. It was during this period that evidence of occult bleeding from the gastrointestinal tract was discovered. Considerable chronic emotional tension was recognized in another patient (case 3), and a fourth (case 4) was constantly worried about his vascular disease.

The acidity of the nicotinic acid preparations administered in large doses is probably the most important (or sole) factor in production or reactivation of peptic ulceration by this drug and probably in other upper gastrointestinal symptoms also. The large doses used for hypercholesteremia would probably lead to gastroduodenal ulceration in more patients if the drug were not administered during or after meals to minimize flushing. We have found plain nicotinic acid to have a pH of 3.5. Aspirin, which is known to be ulcerogenic, has a pH of 2.8. Nicotinamide has a pH of 6.3 but is not effective in reducing cholesterol levels, as previously reported.[6] The buffered nicotinic acid preparation we have used is equivalent to 500 mg. of nicotinic acid per tablet and has a pH of 5.6. Several pharmaceutical modifications of nicotinic acid intended to produce gradual absorption in an attempt to eliminate flushing, have been found to be almost as strongly acid (pH 3.6 to 4.0) as plain nicotinic acid. Even a complex of nicotinic acid with aluminum hydroxide (aluminum nicotinate) had a pH of 4.0, not greatly different from that of plain nicotinic acid.

Because of the solubility of nicotinic acid, it is doubtful that localized gastric erosions are being produced by large particles of tablets, as reported in aspirin-induced ulceration by Muir.[7] This has not been substantiated by gastroscopy or by administering tablets prior to gastrectomy as Muir had with aspirin.[7b]

In addition to the activation of peptic ulcer, upper gastrointestinal symptoms of lesser degree have been present in several other patients. One patient had nausea and vomiting with every nicotinic acid preparation taken, including the buffered preparation, necessitating withdrawal from the study. Five others had nausea with occasional vomiting. The symptoms disappeared when buffered nicotinic acid was substituted for the plain drug, permitting these patients to continue therapy without interruption and without further symptoms.

Our experience leads us to suggest that if large doses of nicotinic acid are to be used for an extended period, it is desirable to use a buffered preparation to prevent peptic ulceration or milder degrees of upper gastrointestinal irritation. This precaution is especially important in persons with a history of previous peptic ulceration, in whom a therapeutic regimen for ulcer should be used as well as buffered nicotinic acid. It is possible that modified nicotinic acid preparations designed to be slowly absorbed from the small intestine may pass through the stomach and duodenum without dissolving, thus eliminating direct chemical irritation of the usual areas of peptic ulceration. Our experience to date does not permit specific comment on this point.

Summary

Activation of peptic ulcer has been observed in five patients receiving large doses (3.0 to 7.5 Gm. daily) of nicotinic acid for hypercholesteremia. Four of these patients had been in the study for

long periods (96 to 124 weeks) when symptoms of ulcer appeared Nausea and vomiting have appeared early in therapy in several other patients, necessitating cessation of treatment in one The use of buffered nicotinic acid permits continuation of therapy without further symptoms or complication in most patients with either activation of peptic ulcer or lesser upper gastrointestinal symptoms If large doses of nicotinic acid are to be used for long periods, it is desirable to use a buffered preparation to prevent gastrointestinal complications This precaution is especially important in persons with a history of peptic ulcer, in whom the usual dietary and pharmacological measures for ulcer are also advisable

Addendum

Since the foregoing report was submitted for publication, two additional cases of peptic ulceration have been discovered Since, like the previous cases, both had severe emotional trauma before developing gastrointestinal symptoms, nicotinic acid is certainly not the sole factor responsible for the development of ulceration and, indeed, may have played a minor role

A 38-year-old man, whose usual dose of nicotinic acid had been 6 Gm daily for the past two years and who had been treated for 130 weeks in all, had always been tense and irritable In January, 1960, he complained of nausea with gnawing distress in the epigastrium when his stomach was empty, relieved by food Roentgenograms revealed a deformed duodenum characteristic of duodenal ulcer No ulcer crater could be identified Treatment with buffered nicotinic acid and an ulcer regimen relieved his symptoms almost immediately After the diagnosis of peptic ulcer had been made, it was learned that his stepson had attempted suicide by shooting himself in the chest two months before the onset of ulcer symptoms

A 47-year-old woman developed nausea and epigastric distress typical of peptic ulcer in January, 1960 She had completed 182 weeks of treatment During the previous two and one-half years, her usual daily dose of nicotinic acid had been 4 5 Gm Roentgenograms revealed a deformed duodenum with an ulcer crater Treatment with buffered nicotinic acid and an ulcer regimen resulted in prompt relief of her symptoms She gave no history of previous symptoms which could be attributed to ulcer She had always been a tense, high-strung person, and her usual apprehension had been increased in August, 1959, at which time a lump in the breast proved to be malignant and required radical mastectomy

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The buffered nicotinic acid tablets used in this study were supplied by the Wampole Laboratories, Stamford, Conn

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TEETH AND THE EUSTACHIAN TUBE—It is elementary to think of the teeth in relation with pain referred to the ear, but it is doubtful if they are often associated in our minds with tubal difficulties Young demonstrated a lymphatic connexion between the teeth and the eustachian tube in monkeys It is possible that the earache of teething infants is often due to a minor otitis media The pink drumhead occurs too often to be ignored, and this may mean an otosalpingitis of lymphborne origin Allied to this condition is the case of the adult patient with periodontal sepsis who comes complaining of deafness This turns out to be of conductive type, and extraction of the offending teeth cures the deafness —R Macbeth, D M Some Thoughts on the Eustachian Tube, *Proceedings of the Royal Society of Medicine,* March, 1960

ACUTE TOXOPLASMOSIS

EFFECTIVE TREATMENT WITH PYRIMETHAMINE, SULFADIAZINE, LEUCOVORIN CALCIUM, AND YEAST

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Acute febrile toxoplasmosis acquired accidentally by needle scratch in the laboratory led to a local ulcer on the finger with bilateral axillary and cervical lymphadenopathy and a fine erythematous rash but no pneumonia Toxoplasma was isolated from the blood stream 9 and 10 days after infection, and antibodies developed Chemotherapy consisting of 25 mg of pyrimethamine and 4 Gm sulfadiazine was instituted on the 9th day and continued for 39 days By the 11th day the patient was afebrile and toxoplasma was no longer isolated Moderate leukopenia and thrombocytopenia were antagonized by 5 to 15 mg of leucovorin calcium and two yeast cakes daily Thus, the drug induced hematological deficiency was reversed by substitution of the inhibited vitamin without need of discontinuing the primary objective, antitoxoplasmic chemotherapy

The synergistic activity of pyrimethamine (Daraprim) and sulfadiazine in acute toxoplasmosis has been amply demonstrated in mice,[1] but direct proof of its occurrence in man is lacking While these agents appear to be effective in the treatment of chorioretinitis of probable toxoplasmic origin,[2] the uncertainty of the diagnosis in individual patients, which requires statistical evaluation,[3] left some clinicians unconvinced of the effectiveness of the drug combination in man An accidental laboratory infection with the RH strain of Toxoplasma provided an opportunity to demonstrate the effectiveness of treatment Likewise, the utility of leucovorin calcium (Leucovorin) and of yeast was shown when it reversed drug-induced thrombocytopenia and leukopenia, thus permitting continuation of antimicrobial chemotherapy

Report of a Case

A 23 year-old laboratory technician, a medical students wife, was admitted to the University of Kansas Medical Center on Jan 24, 1958, complaining of fever, malaise, and tenderness in the left axilla On Jan 15, 1958, the fifth finger of the left hand was scraped with a hypodermic needle containing Toxoplasma gondii The injection series was completed, and thereafter the puncture wound was made to bleed and was washed under a stream of water and was reported only casually to two of her co-workers On Jan 19, she first noted epigastric cramping, which was relieved by eating and did not recur The following morning she awoke with a generalized headache and noted for the first time that she was febrile Chills occurred in the afternoon and on the following day, and her temperature was recorded at 103 F (39 C) The development of symptoms are correlated with temperature records in figure 1 On Jan 22, she reported to a physician who suggested that she had influenza and treated her with aspirin The malaise did not improve and chills and fever persisted On the day before admission she became aware of tenderness in the left axillary region and of a tender, erythematous lesion on the left fifth finger It was then that the accident was recalled and reported On the day of admission the temperature was 102 8 F (39 3 C) and the inflammation of the finger and the tenderness in the axilla had increased A blood specimen was obtained for culture, mouse inoculation, and serologic evaluation The past history revealed negative findings She had worked as a research assistant with Toxoplasma for 18 months The system review was not remarkable except as noted previously

The patient appeared flushed and had a fine erythematous rash on the neck, chest, and arms She was acutely ill when admitted to the hospital Her weight was 120 lb (54 kg) and her height was 5 ft 7 in (170 cm) The blood pressure was 110/70 mm Hg and pulse rate 80 per minute and regular The temperature was 99 8 F (37 7 C) There was a 3-by-3-mm , tender, erythematous lesion with a purulent center on the lateral aspect of the fifth finger of the left hand Results of examination of the eyes and fundi were not remarkable The posterior cervical lymph nodes were distinctly palpable but were not tender Two tender, freely movable nodes, about 2-by-2-cm in diameter, were present in the left axilla A similar, less tender node was discovered in the right axilla The chest was clear to percussion and auscultation The heart was not enlarged to percussion, and no murmurs were heard The liver and spleen were not palpable Abdominal tenderness was not elicited A

From the departments of Pathology and Medicine University of Kansas School of Medicine (Drs Frenkel and Weber) and the Laboratory of Parasitic Diseases National Institute of Allergy and Infectious Diseases Public Health Service (Mr Lunde) neurological examination showed normal findings

Urinalysis showed normal results The hemoglobin level was 13 7 Gm % The white blood cell count was 5,700 per cubic millimeter with 70% polymorphonuclear cells, 6% of which were nonfilamented, 28% lymphocytes, and 4% monocytes

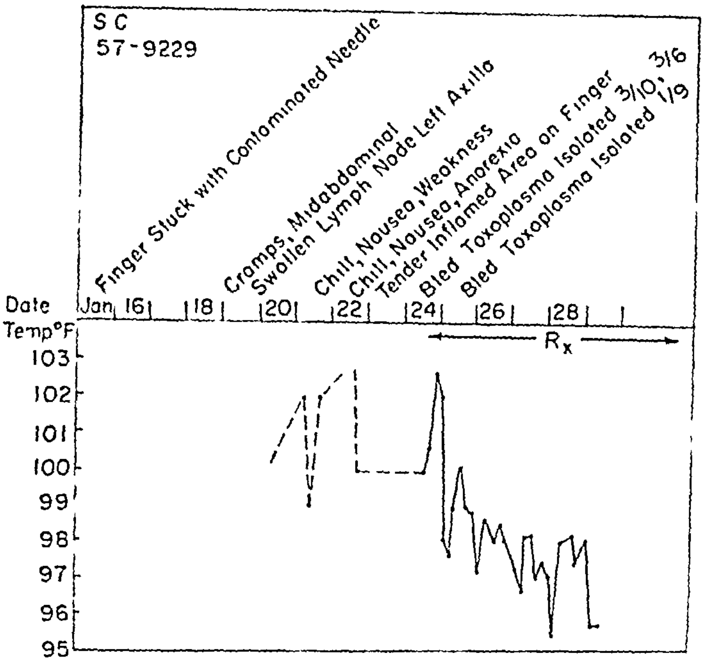

Fig 1 —Chronological sequence of events and febrile course in patient with acute toxoplasmosis

The platelet count was 115,000 per cubic millimeter The hematocrit value was 37 vol % The reticulocyte count was 0 4% The Venereal Disease Research Laboratory test for syphilis showed negative results The blood urea nitrogen level was 10 mg % The blood glucose level was 92 mg % The histoplasmin and tuberculin skin tests showed negative results The heterophil agglutination test showed positive results in a dilution of 1 to 7 Typhoid and brucella agglutination tests and L E cell preparation showed negative findings The sedimentation rate was 9 mm per hour The serum albumin level was 4 1 Gm % and the serum globulin level 2 2 Gm % Electrophoresis showed an albumin level of 47% and the globulin levels as follows alpha-1, 7%, alpha-2, 8%, beta, 18%, and gamma, 20% The total serum bilirubin level was 0 6 mg % The cephalin cholesterol value was 2+, and the thymol turbidity was 2 units The total cholesterol value was 105 mg % with 59% esters The C-reactive protein value was 4+ The chest x-ray revealed a heart of normal size and clear lung fields An electrocardiogram showed normal findings

After the withdrawal of a second blood specimen for mouse inoculation and bacteriological examination, treatment with pyrimethamine and sulfadiazine was started Drug dosages, hematological and serologic responses, and results of animal inoculations are summarized in figure 2 Defervescence was prompt, as is shown in figure 1, the subinflammatory reaction at the puncture site subsided simultaneously Recovery was uneventful, and the patient was discharged on the sixth hospital day Chemotherapy was continued for another 33 days

Infectious Inoculum—A number of hamsters whose acute toxoplasmosis (RH strain) had been treated with sulfadiazine were to be examined for presence or absence of chronic infection The brain and lungs of each of 14 animals had been ground, and the organ suspensions were being injected into mice intraperitoneally in amounts of 0 2 and 0 8 cc Four of these 14 passages done on this day proved to show positive results The recipient mice died after 7 to 10 days, equivalent to an inoculum of from 1 to 1000 LD_{50} (doses lethal to 50% of mice which was equivalent to minimal lethal doses for mice in this instance) The inoculum injected into the patient's finger probably did not exceed 0 02 ml, or from 1 to 100 mouse LD_{50}

Isolation Studies—Toxoplasma was isolated in mice from the patient's venous blood, obtained before treatment was instituted and 15 hours thereafter Of these mice, inoculated intraperitoneally, four died on the 10th, two on the 11th and one on the 19th day By comparison with a titration of this strain in mice this would indicate the presence of from 1 to 10, but less than 100, minimal infectious doses in 0 9 and 0 5 cc of blood None of the mice injected with 0 1 cc of blood developed toxoplasmosis Subinoculation of organs from the surviving mice gave negative results, and the passage mice died in minimal time after injection with Toxoplasma On subsequent passage of the strains isolated, mice were killed three to five days after intraperitoneal inoculation, which was consistent with the behavior of other animals injected with the RH strain in this laboratory Two blood cultures in brain-heart infusion broth, thioglycollate

Serologic Titers in Patient with Acute, Laboratory-Acquired Toxoplasmosis

Date	Time After Infection		Dye Test	Hemagglutination Test*
	Days	Months		
1958				
Jan 24	9		1 4	Negative
25	10		1 16	Negative
26	11		1 16	Negative
27	12		1 32	Negative
28	13		1 64	Negative
29	14		1 256	1 64
Feb 4	20		1 512	1 1,024
7	23		1 512	
13	29		1 256	1 256
20	36		1 1,024	1 256
27†	43		1 1 024	1 256
March 7†	51		1 1,024	1 64
April 15	90		1 16 400	1 1,024
June 13	148		1 16 400	1 4,096
1959				
Feb 10		13	1 4 096	1 4,096
April 6		15	1 4 096	1 1 024
June 12		17	1 2 048	1 4 096
Aug 18		19	1 1,024	1 4 096
1960				
Jan 6		23	1 2 048	1 1 024
1959				
Aug 18‡			1 4,096	1 16 400
Aug 18‡			1 8,200	1 16 400

* —2+ endpoints

† Partial hemagglutination particularly noted in these serums

‡ Baby s cord blood

semi-solid agar, and on pour plates remained sterile for 10 days

Serologic and Immunological Reactions—Antibody development, measured with the dye test [3] and the hemagglutination test,[4] is shown in figure 2 and in the table The specimen obtained nine days after infection contained a titer of 1 4 in the dye test, and the appearance of antibodies in the hemagglutination test lagged five days behind Thereafter titers by the two tests were of a similar order of magnitude The toxoplasmin skin test [3] showed negative results after 20 days and positive results after four months

day, and the platelet count had increased to 176,000 per cubic millimeter on the 25th day, reaching a peak of 268,000 on the 29th treatment day All chemotherapy was discontinued on the 39th day, 47 days after infection The platelet count was found to be 119,000 per cubic millimeter on the 64th day Leucovorin calcium was administered again and the platelet count increased to 178,000 per cubic millimeter one week later Subsequent platelet fluctuations are summarized in figure 2

Subsequent Pregnancy—Eighteen months after infection the patient gave birth to a male infant after an uneventful pregnancy of 298 days The baby weighed 3,675 Gm (8 lb), and the mother weighed (69 kg) 152 lb, prior to pregnancy she had weighed 130 lb (59 kg)

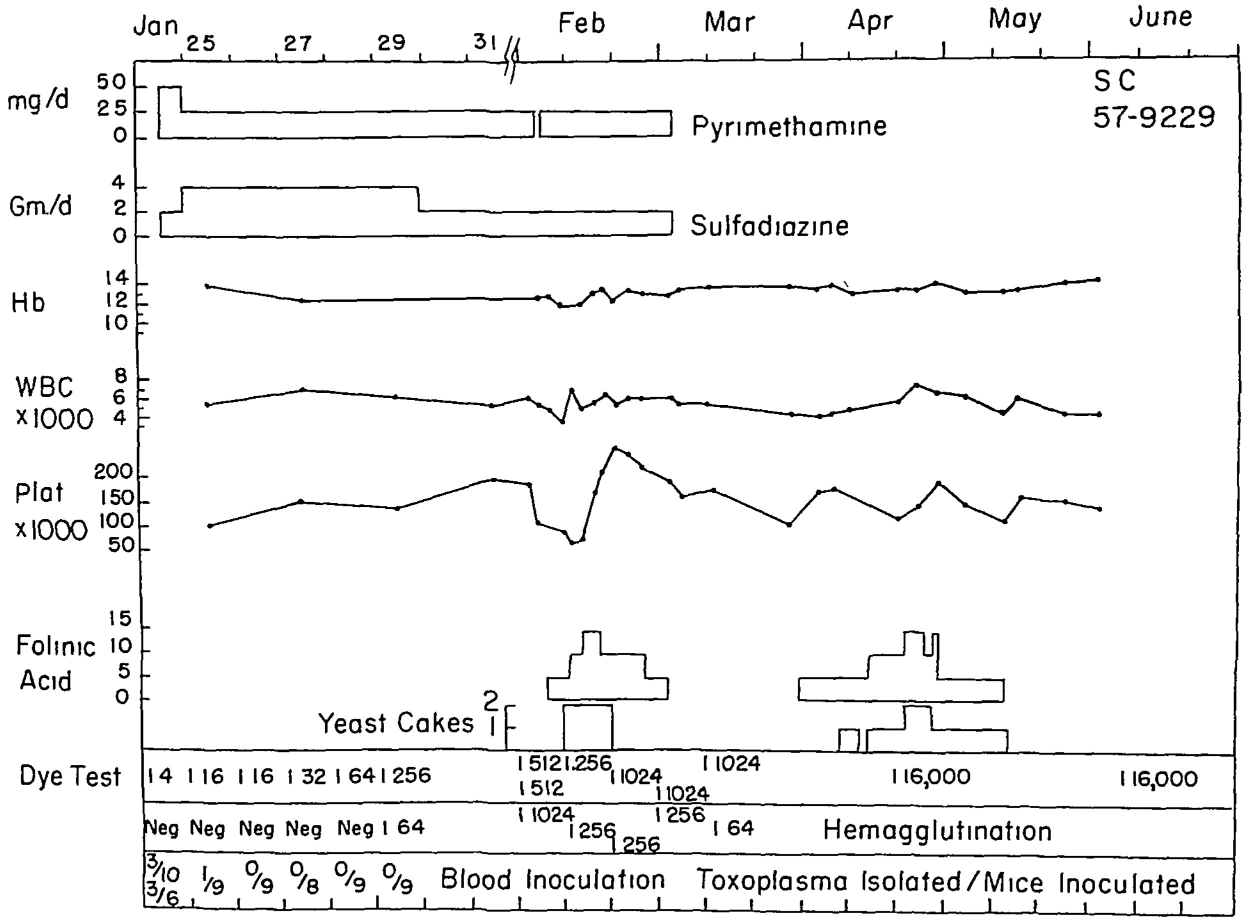

Fig 2 —Correlation of chemotherapy, hematological changes, serologic titers, and isolation studies in patient with acute toxoplasmosis

Chemotherapy and Hematologic Response—On the 13th day of treatment with 25 mg pyrimethamine and 4 Gm sulfadiazine, the white blood cell count was 5,650 per cubic millimeter and the platelet count 128,000 per cubic millimeter On the 18th day the white blood cell count decreased to 3,750 per cubic millimeter and the platelet count to 94,000 per cubic millimeter, the latter was 76,000 per cubic millimeter on the 20th and 22nd day Treatment with leucovorin calcium was started on the 15th day of treatment and treatment with yeast on the 18th day The white blood cell count increased to 7,100 per cubic millimeter on the 20th

Shortly after birth the baby was noted to be cyanotic It died after three and one-quarter days Autopsy revealed an enlarged and dilated cor biloculare (44 Gm) with a single quadricuspid atrioventricular valve and a coarctation of the aorta, proximal to the patent ductus arteriosus, without systemic collaterals Microscopically, no inflammatory stigmas were noted There was passive congestion and edema in liver and lungs The brain and eyes were normal grossly and micro scopically The placenta weighed 745 Gm and was normal grossly and microscopically

Portions of brain, heart, lung, liver, and spleen were inoculated separately into groups of mice Three out of four of the mice inoculated with lung died after one day from bacterial infection The other mice and the remaining mouse inoculated with lung survived Half of these were injected with a virulent strain of Toxoplasma after one month and the other half two months after inoculation Their death was not delayed beyond that of the control mice

Comment

Acute toxoplasmosis of adults has been reviewed in tabular form by Kass and others [5] Recently many cases of lymph node or glandular toxoplasmosis have been described [6] in which mild or moderate febrile reactions were associated with lymphadenopathy, an increase of mononuclear cells or lymphocytes in the blood stream not associated with a heterophil titer but with a rising antibody titer to Toxoplasma In several of these Toxoplasma have been isolated from lymph node biopsies

Sexton and others,[7] Wettingfeld and others,[8] Brown and Jacobs,[9] and Kayhoe and others [10] described laboratory infections of clinical consequence In most of these cases the diagnosis was confirmed by both animal inoculation and serologic response Wettingfeld and others [8] and Kayhoe and others [10] report isolation of Toxoplasma from the blood stream, as was accomplished in our case Chemotherapy appeared to be effective clinically, although this was not documented by daily inoculation of blood specimens into mice as was done with our patient The patient described by Sexton and others [7] died before a chemotherapeutic response could have been expected Wettingfeld's patient [8] was not treated until about two months after infection, and Kayhoe's patient [10] was treated starting 15 days after infection In both Kayhoe's first case [10] and our patient the diagnosis was first substantiated by isolation of Toxoplasma from the blood stream nine days after infection Antibody development was noted on the 11th day, in Kayhoe's first case,[10] when there was a dye test titer of 1 64 Antibodies measurable by the hemagglutination titer showed positive on the 14th day in our case and on the 18th day in Kayhoe's case [10] While the toxoplasmin skin test showed positive results in our patient 4 months after infection, it is interesting to note that it continued to show negative results after 12 and 18 months in the two patients described by Kayhoe and others [10]

The variability in the clinical picture of toxoplasmosis is evident Our case and the laboratory infection described by Kayhoe and others,[10] both with the RH strain, showed an incubation period of five to six days and evidence of antibody development by the 9th to 11th day The case described by Sexton and others [7] had an unknown incubation period, but antibody appeared related to the onset of symptoms However, Brown's,[9] Kass',[5] and Wettingfeld's [8] cases probably showed prolonged incubation periods and delayed appearance of antibody, although exact dates of infection were not known That the early appearance of antibodies is not in itself necessarily related to the presence of clinical illness is indicated by a report by Dr Eichenwald,[11] who observed the appearance of antibody as early as 16 days after a laboratory accident (a titer of 1 256), although the infection was entirely subclinical The cases of glandular toxoplasmosis [6] showed high titers of antibody together with the signs and symptoms of mild infection

A prompt subsidence of parasitemia, along with defervescence and clinical recovery and healing of the lesion at the inoculation site of the finger, was noted upon the initiation of treatment with pyrimethamine and with sulfadiazine Before chemotherapy, Toxoplasma was recovered from two out of two blood specimens (6 out of 16 mice), after chemotherapy, isolation was made from only one of five daily blood specimens in one of 44 mice After the institution of treatment there was only one additional day of fever The lesion of the finger showed decreased inflammatory reaction on the first afebrile day, when the dye test titer was 1 16 and the hemagglutination titer was still negative As the cases with glandular toxoplasmosis show, many untreated patients continue to have symptoms from generalized toxoplasmosis with dye test titers of over 1,000 The same is especially true of patients with toxoplasmosis of the eye or of the central nervous system [3]

It is of interest in this connection to examine the more uniform animal data for the dye test titers associated with subsidence of clinical activity of infection and the acquisition of immunity After vaccination with a low-virulent strain, mice would survive subcutaneous or intraperitoneal infection when antibody titers were between 1 256 and 1 1024 at the time of expected death, as is shown in Frenkel's table 2 [12] Similar antibody titers were associated with effective immunity if infection was delayed by chemotherapy, as is shown in Frenkel's table 4 [12] While it is not possible to make strict interspecies comparisons of the amount of antibody that is meaningfully associated with effective immunity, it would appear unlikely that clinical disease would have abated 11 days after infection without chemotherapy

The beneficial effect of synergistic chemotherapy in toxoplasmosis frequently had been mitigated by the occurrence of thrombocytopenia, which was sometimes associated with leukopenia [3] It has been shown recently that the administration of leucovorin calcium and yeast would correct these hematologic effects even though the administration of pyrimethamine and sulfadiazine was continued [13] It has also been demonstrated in animals that the vitamin and yeast do not interfere with the chemotherapeutic effect against Toxoplasma [13] This patient provides another example of the utility of leucovorin calcium and yeast in facilitating continuation of chemotherapy (fig 2) It might be argued that chemotherapy could have been discontinued safely on Feb 12, when the platelet count was 76,000 per cubic millimeter, since antibody titers were in the range that might indicate effective immunity, however, the results of serologic testing were not known immediately Furthermore, the risk of brain and eye involvement[13] prior to the time when active immunity is adequate in these organs makes mandatory a prolonged course of chemotherapy, as conducted here, until it is known that high stable antibody titers, presumably reflecting the immune status, have been reached

Was there any causal connection between the maternal disease and the fetal malformation? The possibilities of fetal infection, chronic toxoplasmosis of the mother, or drug intoxication will be considered separately

That a chronic latent infection generally follows a nonfatal acute infection is well known from experimental studies in animals[12] and from the occurrence of chronic toxoplasmic chorioretinitis[14] It has also been shown that early persisting infection generally is associated with a high dye test titer and that clearance of infection goes along with a lower or absent titer in mice[12] The persistence of a dye test titer of 1 4,000 13 months after infection strongly suggests a persistent infection in our patient However, this titer, present in the fourth month of pregnancy, would appear to prevent parasitemia, if one judges from animal data[15] Indeed, the blood stream isolations showing positive results in the patients studied by Sexton and others,[7] Brown and Jacobs,[9] and Kayhoe and others[10] were associated with negative dye test findings on these days No inflammatory lesions or stigmata of infection were found in the baby at autopsy or by subinoculation of its organs The baby's antibody titer can be presumed to have been passively transferred from the mother[16] The presence of a higher titer in the newborn than in its mother is occasionally observed[16].

With the etiological chain of the cardiac malformation obscure, one cannot exclude logically the possibility that adverse circumstances resulting from the mere presence of Toxoplasma in the mother or a possible nutritional deficiency caused thereby might result in fetal malformation However, Sabin and others[11] have collected 74 histories of pregnancy in mothers who previously had given birth to a toxoplasmic child and found no increase in fetal morbidity or neonatal mortality In 67 pregnancies there were nine miscarriages and four premature infants, two of whom died In none of these was toxoplasmosis found No instances of congenital malformations were recorded[11] Recently, Dr Heinz Eichenwald informed us that he has observed 216 mothers through a total of 380 pregnancies subsequent to their giving birth to a toxoplasmic baby None of the mothers had received chemotherapy prior to or during pregnancy No infected infants or fetuses were detected, the incidences of miscarriage and congenital defects were similar to a matched control group Hence, there is no evidence that fetal malformations result in association with chronic latent toxoplasmosis in a mother

Fetal malformations have been observed in mice and men after the administration of aminopterin sodium and other folic acid antagonists[17] Pyrimethamine is a folic acid antagonist[16] and is excreted from the body slowly, with traces being detectable in patients' blood for 10 to 25 days after 35 days of administration[18] However, after treatment for 42 days with toxic doses resulting in fatalities in rats, weight gain was resumed promptly after cessation of chemotherapy, and hematologic depression was repaired 21 days thereafter[19] Hence, the interval of over seven months between termination of chemotherapy and conception makes it unlikely that any biologically active amounts of this drug might be present in the body and transferred to the fetus In addition, there had been prolonged administration of leucovorin calcium and yeast after cessation of treatment (fig 2), replenishing body stores of coenzyme F[16]

Summary

Acute febrile toxoplasmosis (RH strain) acquired accidentally by needle scratch in the laboratory caused a local ulcer on the finger, bilateral axillary and cervical lymphadenopathy, and a fine erythematous rash but no pneumonia The diagnosis was proved by isolation of Toxoplasma from the blood stream 9 and 10 days after infection and by the development of antibodies Dye test titers were 1 4 on the 9th day, 1 256 on the 14th day, 1 1024 on the 36th day, and 1 16,000 on the 90th day Antibodies that agglutinated antigen coated red blood cells (hemagglutination test) appeared in a titer of 1 64 on the 14th day and equalled about one-quarter of the dye test titer initially but reached similar levels later on Chemotherapy, consisting of 25 mg of pyrimethamine (Daraprim) and 4 Gm sulfadiazine was instituted on the 9th day after infection and continued for 39 days The patient was afebrile by the 11th day, Toxoplasma was no longer isolated from the peripheral blood, and the inflammatory reaction surrounding the inoculation lesion had decreased rapidly The patient was discharged on the sixth hospital day In the third week of chemotherapy moderate leukopenia (3,750 per cubic millimeter) and thrombocytopenia (76,000 per cubic millimeter) were observed The administration of 5 to 15 mg of leucovorin calcium (Leucovorin) and of two yeast cakes daily resulted in return of the white blood cell count to 7,100 per cubic millimeter and of the platelet count to 176,000 per cubic millimeter on the 25th day Thus, the drug-induced hematological deficiency was reversed by substitution of the inhibited vitamin without need of discontinuing the primary form of treatment antitoxoplasmic chemotherapy

39th Street and Rainbow Avenue (Dr Frenkel)

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CLINICAL NOTES

INSULIN REACTION AND RECOVERY IN DIABETIC PATIENT

REPORT OF A CASE

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A case of severe insulin reaction resulting in unconsciousness of 60 hours' duration was caused in a young diabetic woman by the erroneous administration of 1,800 units of insulin Early recognition of the hypoglycemia and intensive treatment were responsible for the patient's complete recovery

The patient, a 16-year-old, overweight girl, was brought to the emergency room on Jan 3, 1956 after having been unconscious for the preceding three hours This was her 14th hospital admission She had been a known diabetic since 1948, taking about 100 units of insulin daily Her previous admissions had been primarily for diabetic acidosis and coma, of which she had a total of 11 episodes in 1955 alone The patient was dehydrated and restless and responded little to external stimuli Her face was flushed, temperature was 100 0 F (37 7 C), and pulse rate was 120 per minute She did not have Kussmaul's respiration The urine contained sugar (4 +) and no acetone The clinical picture suggested an insulin reaction An intravenous infusion of a 50% solution of dextrose was started, and shortly thereafter blood was drawn for determination of the blood sugar level In the first hour a total of 100 ml was given, and no change was seen in her condition At this point the blood sugar level was reported to be 65 mg per 100 cc (Folin-Wu method) The patient was then admitted, and a 10% solution of dextrose was given intravenously by surgical cutdown, this was necessitated by the poor condition of her veins Dextrose was given continuously for the next 48 hours at a rate of about 3,000 ml per 24 hours Shortly after admission tube feeding was also begun The patient remained unconscious while the blood sugar level ranged from 34 to 88 mg per 100 ml She started responding to continuous treatment 60 hours after admission Her reflexes returned, and she began taking food orally For the next 24 hours, she was disoriented and complained of headache She gradually regained her mental function, and 90 hours after admission in

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From St Vincent's Hospital

sulin therapy was resumed She was discharged on the 10th hospital day

The story elicited by questioning her mother was as follows Two days prior to admission the patient had begun vomiting and had polyuria, drowsiness marked glycosuria, and acetonuria Her physician was consulted by telephone and, having treated her for diabetic coma many times previously, he suggested giving her 100 units of regular insulin hourly, he also suggested that he be called in a few hours if the results of the urine tests or the clinical picture did not improve The mother misunderstood these instructions and thought that "regular insulin" was the lente insulin which her daughter was taking at the time About 1,800 units of lente insulin were given over the next 20 hours, because the glycosuria continued and the drowsiness deepened When the physician was called again he sent the patient to the hospital for admission Apparently she had recovered from the acidosis by means of this dose of insulin and became profoundly hypoglycemic

A follow-up examination made several weeks later did not reveal any neurological abnormality or mental deficiency She was subsequently admitted to this and other hospitals with diabetic acidosis (13 times in 1956) At the time of the writing her condition was satisfactory, blood pressure was normal, and she had no retinopathy or albuminuria

Comment

Many instances of unnecessary administration of insulin in large doses, both erroneously and on purpose, are reported in the literature The clinical picture of hypoglycemia manifests itself in several groups of symptoms arising from the sympathetic nervous system, the central nervous system, and the psychic functions In some instances the patient is able to counteract the excess insulin through glycogenolysis and recovers Usually the hypoglycemic symptoms, especially if neither recognized nor treated, result in coma If the dose is excessive death may result In the fatal cases reported, several histological changes in the brain were described, however, they were not specific Warren and Le Compte[1] concluded that a diagnosis of hypoglycemia as cause of death from the histological findings alone, without corroboration from the case history and the laboratory, is not justified

The danger of hypoglycemia arises from more or less pronounced neurological and mental residua after recovery from these reactions The prolonged hypoglycemia of the brain causes temporary or permanent cerebral damage An unfavorable sign is the prolongation of unconsciousness even after the blood sugar level has been restored to normal or above Baker[2] reviewed the neurological complications caused by various forms of hypoglycemia (erroneous administration of insulin to diabetic patients, islet cell adenoma, insulin shock treatment in schizophrenics, and experimental hypoglycemia in animals) Jones[3] reported three patients with personality changes, mental impairment, and neurological abnormalities that persisted after recovery from the hypoglycemia and suggested the term 'posthypoglycemic encephalopathy' Anderson[4] reported one diabetic who, after four days in coma due to insulin therapy, recovered with residual psychic manifestations and permanent organic damage Allan and Crommelin[5] reported a diabetic girl who, after three days in stupor from excessive insulin dosage, developed hemiplegia, aphasia, and convulsions Gardner and Reyersbach[6] described the case of a diabetic boy who developed progressive mental deterioration and organic brain damage due to repeated hypoglycemic episodes Joslin and associates[7] described a diabetic woman who lost function of the higher cerebral centers after being comatose for almost two weeks, a result of the erroneous administration of excessive insulin

The residual damage is unpredictable and depends on several factors, primarily on total dosage, duration of unconsciousness, frequency of repeated hypoglycemic insults, blood supply to the brain, and cerebral circulation The duration of the hypoglycemia in the reported patients is variable In most cases it is only a few days Raiha,[8] reporting a case in which the patient was unconscious for 2 days, mentions the case of Schleussing and Schumacher in which the patient was unconscious for 72 days and then died Whenever the hypoglycemia persisted for days, recovery without any neurological or psychiatric residua was not frequent In our patient, the early recognition of the reaction and the continuous intravenous administration of dextrose for several days were responsible for her complete recovery The great importance of a continuous supply of carbohydrate to the brain is also shown by Vogl's and Youngwirth's case,[9] in which the patient 63 years of age took a dose of 2,000 units of insulin with suicidal purposes and made a complete recovery as a result of a continuous intravenous administration of dextrose for several days The importance of the cerebral circulation for complete recovery is probably secondary, this is demonstrated by the case just cited and by the fact that in most cases in which residual damage was described it occurred in children or young persons

Differentiation of insulin reaction from cerebrovascular accident or other causes of unconsciousness is important Differentiation of insulin reaction from diabetic coma is of utmost importance for the life of the patient Many reported cases of permanent cerebral damage were caused by failure to recognize the hypoglycemia and by administration of additional insulin to a patient with supposed diabetic coma Clinical features and history provide clues, and every textbook contains a table for differential diagnosis, however, this is not always easy The laboratory is usually of great assistance if one is careful in the interpretation of the results A few words of caution are necessary Demonstration of glycosuria does not exclude an insulin reaction, since the glycosuria may have been caused by hyperglycemia several hours earlier Other substances (uric acid, salicylates, and glycuronic acid) give false-positive reactions for glucose The blood sugar test is available in all hospitals and is usually the best guide, however one should not wait until results are reported, because precious time is lost Laboratory errors cannot be excluded, especially when the emergency conditions under which the test is requested, are considered The carbon dioxide of the blood (CO$_2$ content and alkali reserve) may be influenced by the previous excessive intake of sodium bicarbonate or other alkalizing agents which cover up a depressed carbon dioxide content in diabetic acidosis, hence, treatment may be delayed If laboratory results strengthen the clinical impression, they are acceptable, otherwise the tests should be repeated The qualitative plasma acetone test is reliable in experienced hands If doubt exists as to the diagnosis in an unconscious diabetic patient, it is always safer to give dextrose intravenously (10 to 20 ml of 50% solution) and watch for prompt improvement or wait for the final word from the laboratory

Confusion with respect to the terms "regular" or "clear insulin," meaning the unmodified crystalline insulin, as occurred in our case, may happen more frequently than is expected, particularly among persons not well versed in the care of their diabetes The diabetic and his relatives who have been well indoctrinated in the basic principles of diabetic care enjoy a definite advantage

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EARLY DETECTION OF PREECLAMPSIA

HOME TESTING WITH COLORIMETRIC PAPER STRIPS

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Proteinuria, edema, and an increase in the diastolic pressure, which occurs in the latter months of pregnancy, are well-established indications of preeclampsia Of these findings, consistent proteinuria is considered most important because it is usually detectable before other signs of preeclampsia appear and because the quantity of protein excreted generally parallels the severity of the condition Success in the management of the preeclamptic patient is markedly enhanced by its earliest possible diagnosis Consequently, it is clinically essential to test for proteinuria frequently

It is our routine practice to see all uncomplicated obstetrical patients in the office or the clinic at monthly intervals during the first two trimesters, every three weeks during the seventh month, every two weeks during the eighth month, and weekly during the final month Testing for proteinuria during these visits is done routinely However, patients do develop toxemia, sometimes to a marked degree, between visits

For about a year, we have used a procedure that is designed to expedite the earlier detection of preeclampsia by having patients test their own urines for proteinuria daily or every other day at home with use of the colorimetric paper strip Such home testing became a very simple procedure with the availability of a colorimetric paper strip (Albustix) test The test paper is a bibulous strip of cellulose which has been impregnated with tetrabromphenolphthalein blue and citrate buffer This protein test is based on the well-known phenomenon of a "protein error of indicators" which involves the fact that at a fixed pH certain indicators will have one color in the presence of protein and another color in the absence of protein The citrate buffer provides a hydrogen iron concentration of about pH 3 At this pH, tetrabromphenolphthalein blue has a yellow color which in the presence of increasing amounts of protein will have a green to blue color The color of the test strip, when compared to the color blocks of the Albustix color guide, permits semiquantitative appraisal of proteinuria

Home testing was reserved for those patients

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Read at the Dr Milton J Goodfriend Clinical Day, March 24, 1960 with histories of previous episodes of toxemia and those having one or more of the signs potentially indicative of preeclampsia Occasionally this procedure was advised when the patient, for some reason or another, was unable to assure keeping her office or clinic appointments In the majority of cases, home testing was employed only during the last trimester

Our patients were instructed to moisten the test strip by quickly passing it through the latter portion of the urinary stream, being careful not to allow the strip to come into contact with the genitalia As many of the clinic patients were below average intelligence, the color block representing a protein concentration of 100 mg per 100 ml was pointed out to them Patients were instructed to report at once any test strip color equalling or exceeding the color of this block

Among the first 50 patients who were requested to perform tests for proteinuria, one patient exhibited a significant positive reaction This patient, two years previously, had had an antepartum fetal death associated with preeclampsia in her first pregnancy During this pregnancy, she was maintained on a salt-free diet and diuretics throughout the last trimester At weekly clinical visits, there was no sign of edema, her blood pressure was normotensive and no albuminuria was seen On her last visit, the blood pressure was recorded as 104/60 mg Hg and urine negative Two days later she called to report that her test reading was 4+ (protein over 1,000 mg per 100 ml) She was immediately hospitalized and found to have a blood pressure of 178/90 mg Hg and a 4+ albuminuria, checked by several methods She responded favorably to therapy, and four days later labor was induced with oxytocin injection (Pitocin) given intravenously and terminated by a normal delivery of a healthy female baby weighing six pounds The postpartum course was uneventful for both the mother and child

It is reasonable to assume that had she not detected the proteinuria, a five days' delay would have occurred before her condition would have been detected at her next scheduled visit As so often happens within this short interval, a severe grade of toxemia may result before initiating therapy The potential risk involved in such a delay is well established and may have resulted, in this case, with a second stillbirth

We consider that home testing for proteinuria is a practical method for pregnant women to expedite the diagnosis of preeclampsia between prenatal visits The colorimetric paper strip test for proteinuria was very suitable for this purpose In every instance, the usual clinical laboratory method of testing for albuminuria corroborated the paper strip test

Initially, it was feared that patients might not cooperate with the home testing program or would be overly alarmed if any color developed on the protein test strip This was not the case, however, and instead, patients felt that they were now actively participating in their prenatal care and expressed a sense of security by noting daily that their urines were either free from protein or did not contain enough to require reporting Patients expressed their pleasure over the home testing program because they believed that they were getting better prenatal care It is our conclusion that they were

Summary

Fifty patients with possible toxemia of pregnancy or with a history of previous toxemia were given colorimetric paper strips for home testing Albumin was detected by one patient between visits which resulted in earlier toxemia therapy The method is proposed as adjunctive laboratory testing for the earlier diagnosis of preeclampsia

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Dr Norman L Hemmway of Ames Company Inc, supplied the Albustix used in this study

FRACTURE OF THE MONTH

FRACTURE OF THE TIBIA AND FIBULA

PRESENTATION OF CASE

Otto E Aufranc, M D , Boston

Dr J H Dixon A 51-year-old maintenance man was admitted to the emergency ward of the Massachusetts General Hospital in November, 1958 one hour after being struck by an automobile He was conscious and not in shock The right leg, which had been wrapped in a pillow splint, revealed an open transverse fracture of the midshaft of the right tibia and fibula (fig 1 and 2) The bone was exposed from the anterior tibial tubercle to 2 cm above the ankle joint, and the skin was sleeved circumferentially over this area Sensation and circulation were present in the foot, and the dorsalis pedis pulse was palpable, the posterior tibial pulse was absent The wound was grossly contaminated with clothing and dirt, and there was little bleeding from the area No other significant injuries were present The patient had always been in ex-

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From the Massachusetts General Hospital

cellent health prior to the accident He had had no previous immunizations

Discussion of Treatment

Dr W MacAusland Jr This severe soft-tissue injury must first be discussed with reference to the entire patient Appropriate therapy aimed at combating primary shock and preventing secondary shock should be instituted, and fluids should be intravenously injected immediately with a no 18 needle A transfusion of whole blood should be started as soon as possible The patient should be placed in a mild Trendelenburg position and assigned to a 10-minute vital sign chart A careful and thorough general physical examination should be rapidly undertaken, with particular attention to possible occult injuries of the abdomen, chest, and cranial vault The wound should be covered with sterile dressings and gentle compression applied if there is arterial bleeding While the pillow splint is still on, appropriate x-ray films should b obtained, including one of the joint above a below the fracture Immediate arrangements mu be made for surgical débridement

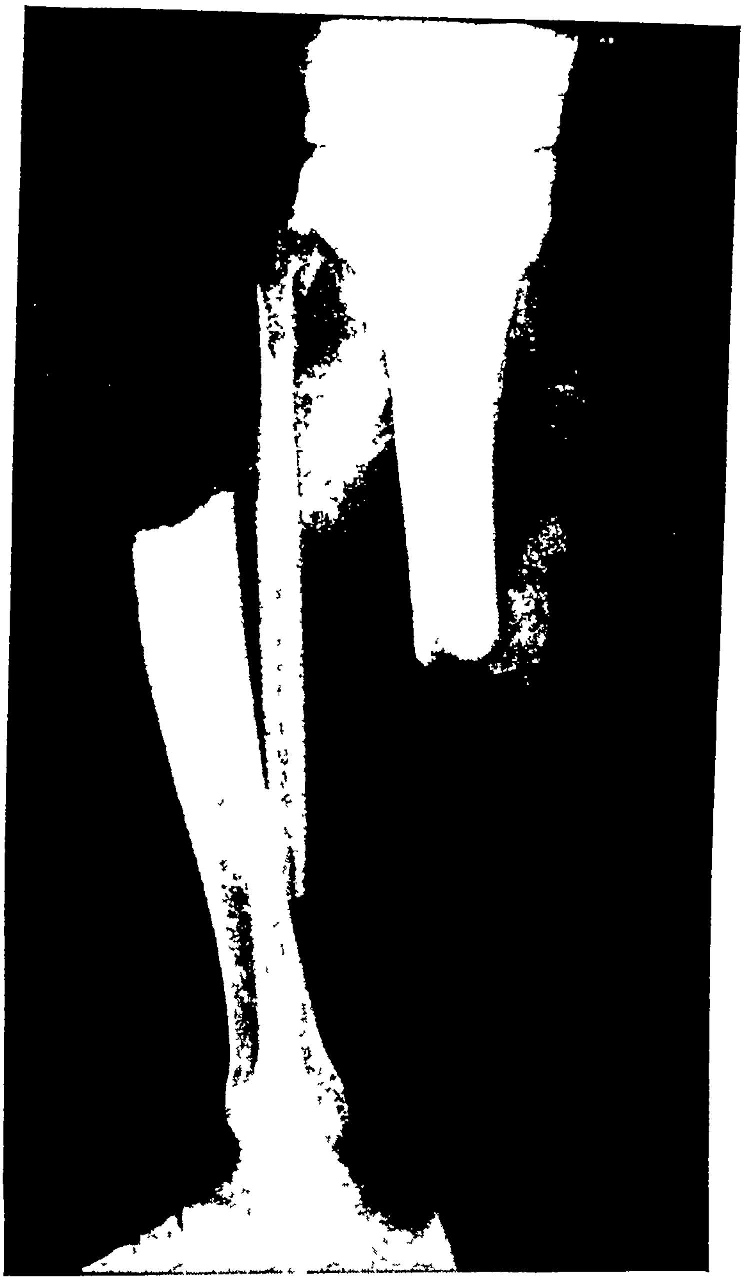

Fig 1 —Roentgenogram November, 1958, of transverse fracture of midshaft of right tibia and fibula note wide separation of fractured ends Air or gas in tissues reflects extensive soft tissue damage and muscle stripping from bone

Further preparation of the patient for surge should include tetanus prophylaxis If the patie has been previously immunized, 1 cc of tetan toxoid should be administered, otherwise 3,0 units of tetanus antitoxin should be given for wound of this magnitude Prophylactic admini tration of antibiotics is to be recommended, pa ticularly penicillin, for prevention of possible g gangrene The use of at least 500 cc of who blood prior to surgery would be beneficial, b this should not delay surgery

Anesthesia —This particular patient is best ha dled with a general or spinal anesthesia

Treatment in the Operating Room —The injur leg should be constantly steadied by appropria assistance to prevent additional damage While is held, it should be rapidly shaved and wash with sterile saline and green soap solution, the soap should be prevented from actually entering the open area by the use of handkerchiefs and sponges The extremity can then be carefully prepared with an appropriate iodine-alcohol solution or a simil

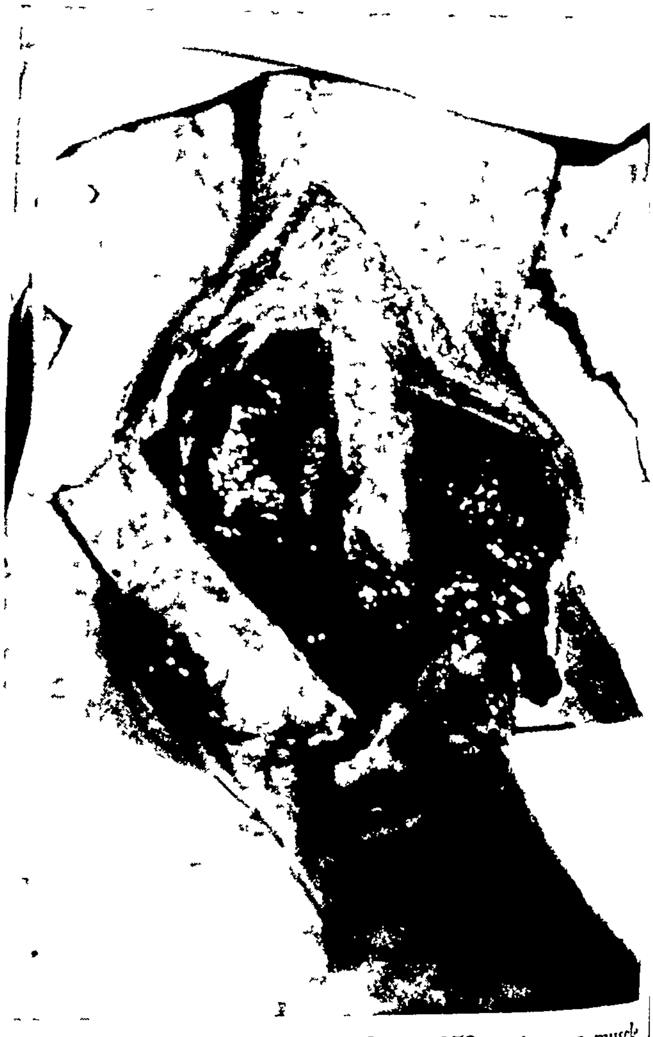

Fig 2 —Photograph, November, 1958 extensive muscle laceration suggests need for exceptional care in debridement Irrigation of wound can be kept to minimum if debridement is meticulous

solution of one's personal choice The entire extremity should be draped free The lower leg should be placed on an irrigating basin and irrigated with sterile saline solution to wash out all loose and gross dirt

Skin Treatment—The skin should be carefully débrided of its necrotic edges All viable skin that is salvable should be saved Skin edges should not be excised freely just for the sake of excision

Soft Tissue Treatment—The surgeon must remember that hemorrhagic muscle itself looks necrotic, but he must first determine if it actually is No necrotic muscle should be left, if possible Necrotic muscle, which does not contract when pinched with a forceps and does not bleed, is débrided with a scissors

All nerves are carefully preserved and are not excised under usual circumstances If the nerves are severed, they are sutured, if possible, otherwise, both ends are marked with a fine wire suture for future ease of identification at reexploration

Treatment of Bone—With adequate excision of skin and necrotic muscle, the fracture may be reduced and held with a bone clamp to provide stability and prevent further soft tissue damage With the bone edges clean and the fracture reduced in this particular type of fracture, I would personally favor the use of an intramedullary Lottes nail Although I am well aware that there was gross contamination of the wound, the risk is justifiable, considering the excellent fixation that is bound to occur with this transverse midshaft fracture Rigid stability of the fracture will aid immeasurably in the management of the soft tissue wound and in the prevention of further bleeding and edema during the frequent changes of cast and dressings which undoubtedly will be required

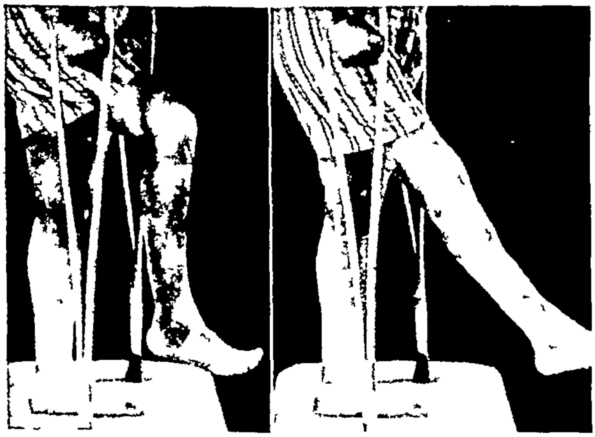

Fig 3—Flexibility of knee and foot has steadily increased since roentgenogram, and clinical evidence of bony union has appeared

After the insertion of the Lottes nail, the skin is closed loosely With a wound of this size, the skin edges should never be drawn together under any undue tension, because further edema and soft tissue swelling are bound to occur The bone, in particular, should be covered with skin The use of relaxing incisions may be particularly appropriate, but this is determined only at the time of skin closure If required, I would favor a relaxing incision The resulting defect should be covered with a split-thickness graft As amputation may be required, the donor site for the graft should come from the opposite thigh, thus avoiding any possible difficulty with a painful thigh scar at the site of prosthesis contact Dry sterile dressings are then applied A long leg plaster cast from toe to groin, which is immediately split, concludes the operative treatment

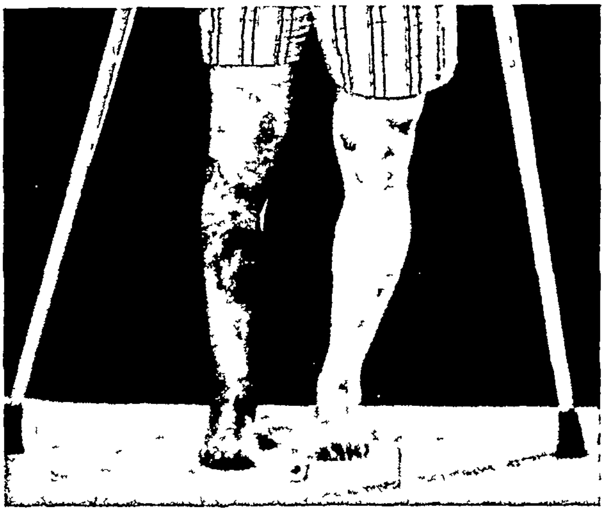

Fig 4—Maintenance of excellent fixation and alignment increases usefulness of the extremity

Administration of appropriate antibiotics of one's individual choice, probably penicillin and streptomycin, should be continued In the first few days the surgeon must be particularly observant for the development of gas gangrene by the careful inspection of the cast and thigh and by hourly observation of the temperature, pulse, and respiration Daily determination of the hemoglobin level should be done for the first few days, and the leg should be constantly elevated

Dr E E Record I agree in every detail with Dr MacAusland's discussion of the suggested treatment of this severe fracture I would like to emphasize the importance of internal fixation of a fracture of this particular type, which by immobilization will provide a maximum opportunity for wound healing and for preservation of circulation by preventing any further compression or buckling of those vessels which have not already been damaged by the initial injury In this instance, the wound was extremely dirty, and extensive debridement was necessary The skin was closed primarily, such conditions demand frequent, early inspection of the wound so that, at the earliest possible moment, wound breakdown will be detected and immediate steps can be taken for adequate drainage of the area involved

At the time of débridement, it was noted that the skin of the lower leg had been almost completely avulsed in a sleeve-like manner For optimum healing of such avulsion of the skin, firm but gentle compression should be applied to the lower leg, which is in a well-padded cast In order to preserve the skin contact with the fascia and muscle layers, a posterior stab and drainage wound should be made to prevent a hematoma from forming

Treatment

Dr J H Dimon We believed that an attempt to save the leg was indicated At the same time we fully realized that amputation might become necessary at any time in his immediate postoperative period if spreading sepsis or gangrene developed We also realized that perhaps amputation might be necessary later on in this patient's course

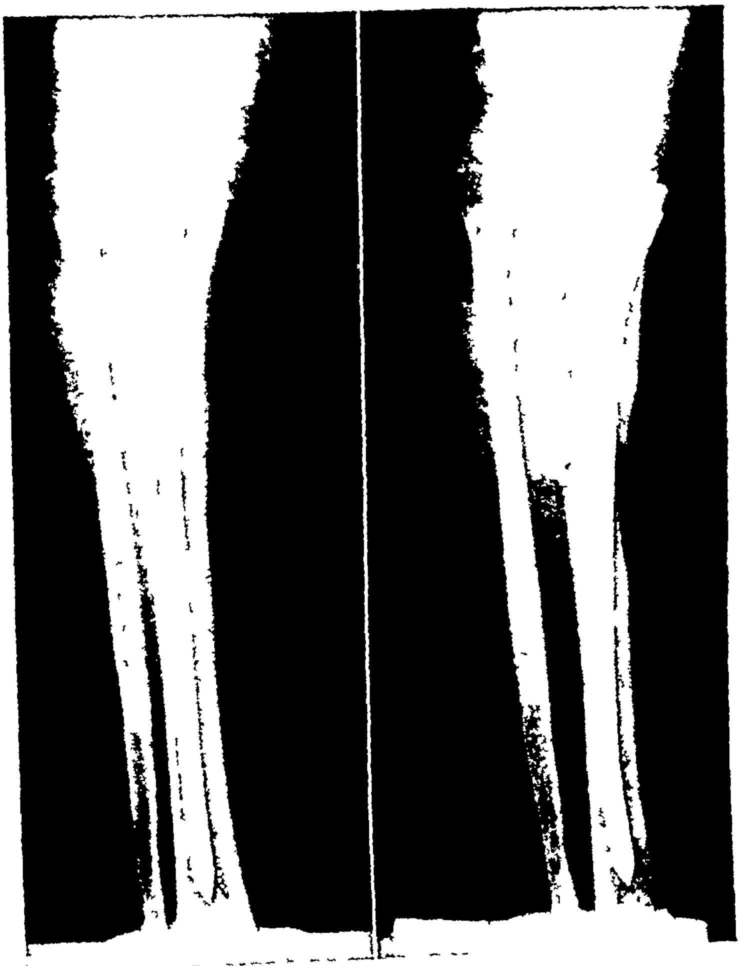

Fig 5—Roentgenogram, February, 1960 excellent alignment revealed may give false sense of security in postoperative management

After appropriate intravenous therapy had been begun and after a sterile dressing and a pillow splint had been applied in the emergency ward, the patient was immediately taken to the operating room Penicillin, streptomycin, and 3,000 units of tetanus antitoxin were likewise administered in the emergency ward In the operating room the wound was thoroughly irrigated and débrided A Lottes nail was introduced to maintain reduction of the fracture It was possible to close the skin primarily without undue tension Because of the circumferential sleeving of the skin about the entire lower leg, anteromedial and posterolateral Penrose drains were inserted, and the patient was placed in a long leg cast which was constantly elevated

He was treated postoperatively with intravenously administered chloramphenicol (Chloromycetin) and penicillin and streptomycin, given intramuscularly He was watched carefully for signs of gas gangrene or spreading infection, however, his postoperative course was one of continued improvement On the second, fifth, and ninth postoperative days, we changed the cast and dressings in the operating room An area of slough approximately 7½ cm long and 1 cm wide developed over the fracture site, which became a chronic draining area, the bone and Lottes nail being exposed

He began crutch walking, with partial weight bearing, in a long leg plaster cast two month after injury and was discharged at two and one half months Five months after injury he ha motion at the fracture site, as seen in the expose area He continued on partial weight bearing, wit crutches, and nine months after injury a parti sequestrectomy and split-thickness grafting wer performed at the site of drainage The grafts di not take, and drainage continued X-ray films tak at nine months suggested that union had occurr posteriorly, and he was allowed partial weig bearing without the cast

Follow-up Study 17 Months After Injury

Dr J H Dimon The patient is walking, be ing an estimated 60 to 100 lb of weight on leg There is a slight amount of drainage from t fracture site, which requires a daily dressing the patient He has full extension of the kn (fig 3 and 4), 65 degrees flexion, and no pa X-ray films show apparent union (fig 5) We f that the Lottes nail should be left in indefinite until there is no question that the union is stu enough to allow its safe removal and sequestr tomy, if indicated

Dr O E Aufranc The most immediate d sion in an injury like this is whether to amput With adequate distal circulation and sensation decision to save the leg is obvious With such extensive sleeving or a complete circumferen separation of the skin from its deep fascia, use of a relaxing incision did not seem advisal The small margin of slough of skin was expec to be greater than it actually was Once it is cided to save the leg, this plan should be follow for a reasonable length of time In this instan the length of time is longer than with the us transverse fraction of the tibia As long as the lo condition of the fracture and other tissues does seem to be getting worse, it may be assumed be getting better The emphasis here seems to to hold on as long as things do not appear to getting worse

COMMITTEE ON COSMETICS

Report to the Committee

The Committee on Cosmetics has authorized publication of the following report

VERONICA LUCEY CONLEY, Ph D , *Secretary*

USE AND ABUSE OF PSORALENS

S William Becker Jr , M D , Chicago

The psoralens[1] are furocoumarins to which most people in the United States have been exposed Celery contains psoralen Oil of bergamot, widely used in perfumes, contains 5-methoxypsoralen Thus, there are few persons who have not ingested psoralen and probably no adult woman who has not applied a psoralen to her skin Plants containing psoralen have been used to produce pigmentation for at least 3,000 years Recently, oil of bergamot has been used for this purpose Scientific investigation of the psoralens began when Kuske[2] and, later, Fahmy and his group[3] isolated the active chemicals from a variety of plants Many physicians in different countries began to study these compounds Lerner, Denton, and Fitzpatrick[4] and Kelly and Pinkus[5] initiated clinical evaluation in the United States

The chemical alterations in the psoralens which occur after oral ingestion or topical application to the skin are not known Exposure of psoralen solutions to ultraviolet light results in the formation of new compounds[4] External application or oral ingestion of small amounts of psoralens appears to have no effect in humans unless followed by exposure to ultraviolet light Fitzpatrick and others[6] showed that the psoralens act as photosensitizers, not only increasing the response of skin to light but altering the wavelengths to which the human skin responds Normally, light with wavelengths longer than 3,200 A has no effect on the skin After sensitization by the psoralens, burning and tanning are produced by light with wavelengths as long as 4,000 A[7]

After oral ingestion of the psoralens, the skin becomes photosensitive in about one hour The peak of this sensitivity is reached in two hours and disappears in eight hours The application of a psoralen solution on the skin produces greater sensitivity than does oral ingestion The skin may remain sensitive to sunlight for several days Increasing the dose of the psoralen increases the photosensitivity but does not appear to affect the duration of the reaction Twenty milligrams of methoxsalen (8-methoxypsoralen) or the equivalent dose of other psoralens approaches the limit of tolerance of the skin, larger amounts commonly result in blistering In sub-blistering doses, variations in the amount of psoralen and sunlight do not alter the reaction Small oral doses (5 mg of methoxsalen) followed by prolonged exposure to sunlight and larger oral doses (20 mg of methoxsalen) followed by shorter exposure to sunlight produce the same changes in the skin

Only a few of the many psoralens have been used clinically The original commercial preparation contained methoxsalen and 8-isoamylenoxypsoralen The product presently available in the United States is methoxsalen Investigations have been carried out with 5-methoxypsoralen and trimethylpsoralen Preliminary studies indicate that trimethylpsoralen is the most potent of this group It appears to be about twice as potent as methoxsalen

Light Source

Each photoreactive chemical has certain wavelengths of light which produce the greatest activation These wavelengths are not definitely known for the psoralen intermediates, and results cannot be predicted if light of a limited spectrum is used The basic responses of psoralen-sensitized skin to sunlight and broad-spectrum ultraviolet lamps are known The ultraviolet lamps approach, but do not duplicate, the spectrum of the sun They lack the energy available in natural sunlight Natural sunlight is, therefore, the preferred light source for use with the psoralens

Therapeutic Effects

Miescher[8] demonstrated that after exposure to sunlight the stratum corneum epidermidis (horny layer) thickened This, rather than the production of pigment, provides the initial protection against sunburn The psoralens have a pronounced effect on this reaction[9] In psoralen-sensitized skin, the stratum corneum becomes thicker and denser than normal A red staining homogenous layer, resembling the stratum lucidum seen in the palms and soles, develops at the base of the stratum corneum Increased density and formation of stratum lucidum rather than simple thickness, appear to be responsible for increased resistance to ultraviolet light[10] Only small doses of psoralen (5 to 10 mg of methoxsalen) and suberythema sunlight are necessary to produce this change The stratum corneum is

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altered in normal skin after about two weeks of exposure to sunlight. Skin normally more sensitive to sunlight takes longer to change. Erythema accelerates the change, but no protection develops if there is blistering or peeling. The change occurs only in the areas which are exposed to the sun. This alteration of the horny layer of the skin persists in normal persons for at least six months and provides lasting protection against ultraviolet rays.

Persons with albino skin and various types of leukoderma can be protected against sunburning.[11] Use of the psoralens has revealed that some light-sensitive persons, mainly those with red hair cannot easily alter the stratum corneum. Prolonged use of the psoralens will produce some protection, but, frequently, this is not enough to prevent sunburning.

The psoralen-induced thickening of the stratum corneum helps protect persons who are allergic to sunlight.[10] The efficiency of the protection depends on the person's sensitivity and the wavelengths of light to which they react. The psoralens must be used with minimum exposure to ultraviolet light, so that the stratum corneum can be thickened without producing clinical inflammation. Since protein cannot completely absorb light sensitive persons will derive only partial protection. Light of the longer wavelengths penetrates more readily than light of the shorter wavelengths. Protection will be greatest when the patient is allergic to short and medium ultraviolet wavelengths rather than to long ultraviolet wavelengths or visible lights.

Pigmentation

The psoralens are not primary pigmenting agents.[9] Ingestion of psoralens without exposure to ultraviolet light will not cause pigment formation. Ultraviolet irradiation produces pigmentation only if there is an inflammatory reaction, which results in the formation of melanin. The psoralens influence clinical pigmentation by virtue of the altered stratum corneum. Melanin normally leaves the skin with the exfoliating horny layer. The adherent and compact stratum corneum induced by psoralens becomes filled with melanin. Melanin is also seen in the basal cell layer. It is not certain whether this latter pigment is the result of a retention phenomenon. Psoralen-altered skin will retain more pigment than does normal skin. The "psoralen tan" is, therefore, darker than the normal tan but it is not permanent and slowly fades. Melanin also protects the skin against sunburn. The psoralen-tanned skin has double protection against the sun.

Diseases Responding to Sunlight

Acne vulgaris, psoriasis, and many eczemas respond favorably to sunlight. Many of these conditions have been treated with photosensitizers of the coal tar group and ultraviolet light. In my experience, use of the psoralens will increase the therapeutic effect in any disease responding to sunlight. The psoralens are potent photosensitizers and should not be used in the acute stage of eczema but only in the subacute or chronic stages. Since it is necessary to produce inflammation to obtain healing, the patient will develop a tan. The altered stratum corneum which protects against sunlight hinders therapy of disease. After several weeks of therapy, the patient becomes resistant to ultraviolet. The exposure time must then be increased. It is at this time that sunlight has its greatest advantage over relatively weak sunlamps.

Leukodermas

Study of the disease vitiligo has been primarily responsible for medical interest in pigmenting agents. In dark-skinned races, this disease is a serious cosmetic defect. The cause of vitiligo is unknown,[12] but there appears to be inhibition of the tyrosinase system to varying degrees. Since the inhibitory chemicals are not known, specific effects of the psoralens cannot be evaluated. The psoralens and sunlight appear to affect vitiligo through the production of inflammation. Therapy must be carried to the point at which the depigmented areas become red and the normal skin tans before repigmentation of vitiliginous spots occurs. New pigment usually appears about the hair follicles and slowly spreads. The response of patients with vitiligo is variable. A few patients derive no benefit, some develop new pigment but lose this after therapy has stopped, and some develop new pigment and retain it through the winter so that each year more pigment can be added. Complete cures of vitiligo have been infrequent. About half of the treated patients obtain an appreciable amount of new pigment.[13] It is always possible to protect the depigmented areas against sunburn. Although the psoralens are not perfect agents for vitiligo, they are the best presently available.

Patients with complete or partial albinism have irreversible defects of the tyrosinase system and cannot acquire pigmentation by the use of the psoralens. Severe inflammations, accidents, surgery, and burns lead to destruction or inactivation of the pigment-forming cells. The resultant leukoderma is not affected by psoralen therapy. Many mild inflammatory reactions leave temporarily depigmented areas. Repigmentation of these areas is accelerated by the psoralens.

Skin Cancer

Sunlight is a definite factor in the production of skin cancer.[14] The mechanism by which sunlight leads to malignancy is not known. Experimental evidence[15] shows that, in mice, intraperitoneal injections of relatively large amounts of psoralen increased the number of sunlight-induced cancers, smaller amounts of psoralen added to the diet decreased the number of cancers. These findings cannot be directly applied to the human because of biological differences. We know that, whereas Caucasoid skin develops solar carcinoma, Negroid skin is almost immune. The most obvious difference between Caucasoid and Negroid skin is the presence of melanin in the basal cell layer Ultraviolet irradiation results in a migration of melanin to the upper layers of the skin If the availability of melanin is the basis of resistance in the Negroid skin, then psoralen-tanned Caucasoid skin would be expected to have similar resistance The psoralens are now undergoing testing for use in the prevention of cancer,[15] but no definite results are detectable as yet

Toxicity

Nausea, vomiting, vertigo, and mental excitation have been produced by use of the psoralens These symptoms are more frequent with administration of larger doses (20 mg or more of methoxsalen) and often disappear when the dose is reduced There has been considerable concern over changes in liver function tests during psoralen therapy Liver function in normal subjects was unaffected by use of methoxsalen [16] Elliott,[13a] however, found that results of liver function tests were abnormal in a few patients At present, psoralens should be used cautiously in patients with obvious or incipient liver disease Toxicity of the more potent trimethylpsoralen is not yet known

Abuses of Psoralens

Early publicity labeling the psoralens suntan pills' has led many physicians and patients to regard these compounds as an equivalent to proprietary suntan lotions Semantics unfortunately may have a greater influence than facts In reality, they are potent photosensitizers Casual prescribing, inadequate instructions to patients, passing around the medication, and experimentation by patients have all led to instances of severe, blistering dermatitis Light allergy must be carefully differentiated from simple tendency to sunburn Use of the psoralens has precipitated allergic solar dermatitis in some patients The eyes, which become sensitive to ultraviolet after ingestion of psoralen, must be protected from bright sunlight The psoralens sensitize the eyes to some of the wavelengths of light given off by fluorescent bulbs Patients must be cautioned about working under intense artificial illumination while sensitized by psoralens The psoralens must be used in the tolerated range if protection is desired The protection depends on altering the horny layer of the skin If peeling or blistering is produced, the patient becomes more sensitive to sunlight instead of less sensitive The dosage of psoralen and sunlight must be adjusted to the individual patient There is no single schedule which will fit every type of skin and the sunlight in every locality

Comment

The psoralens have been established as potent, controllable photosensitizers They can be used to increase or decrease the effects of sunlight in the human skin They are a valuable research tool in the study of the responses of the skin to ultraviolet light Several papers have indicated that the psoralens are activated by the energy of x-ray irradiation and may protect the patient against deleterious effects of x-ray [17] This reaction probably involves a different mechanism than the response to ultraviolet light It would be better to consider the psoralens under the rather broad title of energy absorbers Their full effect on the electromagnetic spectrum remain to be evaluated

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THE JOURNAL
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FRACTURE OF THE MONTH

SINCE prehistoric times the teaching of medicine has been by precept and example. Before the establishment of formal medical schools, apprenticeship to a senior physician was the only means by which a young man could get a medical education. This came through practical experience. Case presentations became a part of medical teaching in medieval times, when Taddeo Alderotti (1223-1303) at Bologna introduced a new form of medical literature called "consilia." These were discussions of clinical cases, giving a description of symptoms and full details of treatment. The case method of teaching has stood the test of time for centuries, it has been used in the law as well as in medicine. Fractures lend themselves well to this type of instruction, and amazingly accurate presentations of certain fractures were given by Percivall Pott (1713-1788 and Abraham Colles (1773-1843) even before Roentgen's discovery of the x-ray in 1896.

Since the turn of the century, due largely to the advent of the x-ray film, the diagnosis and treatment of fractures and dislocations have been revolutionized. Two world wars have also contributed greatly to our knowledge of wounds and the great expansion of orthopedic surgery since World War I has come about largely because of experience with battle casualties, by a study of the individual problem at hand or of a group of cases followed to the end-result. Fractures can be studied perhaps more accurately than any other form of injury or disease, they can be finally evaluated from the points of view of restoration of normal anatomy, by the x-ray film, function restored to the part, and economic recovery, according to the return of the patient to his pre-injury earning capacity.

The first fracture clinic in America to carry out such end-result studies was established at the Massachusetts General Hospital in 1917. It is fitting, therefore, that this new, yet old, form of teaching presented in the "Fracture of the Month" in this issue should be initiated by that Clinic.

The idea of this presentation was originated by the present chief of the clinic, Otto E. Aufranc, but more than one person will be involved with the cases to be discussed. It is hoped that the case presented will not only convey to the reader the details of diagnosis and treatment of the problem at hand but will also teach principles involved in the management of wounds to bone and to soft parts.

The Cabot case histories, initiated by Richard Cabot at the Massachusetts General Hospital in 1915, have been and are a recognized form of postgraduate teaching throughout the world. This method of clinical presentation has been copied by many clinics and by several journals. We dare predict that the "Fracture of the Month" will fulfill the same need in teaching the diagnosis and management of injuries to bone.

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Boston 14

DOCTOR VIS-A-VIS POET

Frederick von Schiller, Oliver Goldsmith, and John Keats are examples of illustrious poets who chose a career in medicine before they deviated to another professional path. Exposure to 18th or early 19th century literature probably began in college for most of us. A few learned of Keats and Shelley in the home when reading from the Bible before breakfast, reading from the literary masterpieces that reposed on the shelves of the front parlor, or serious supper conversation over contributions to *Harper's Weekly* and the *Atlantic Monthly*, was proper. Most every physician has read Gray's "Elegy Written in a Country Churchyard." Not all have understood the implications. Possibly the "beatnik" of the 18th century could have interpreted word, phrase, and paragraph correctly, or incorrectly, depending on his obtuseness, but interpreted it nevertheless.

Walter A. Wells[1] has described the medical findings of the events leading to the death of John Keats, the greatest 19th century poet, but has made no pretense of interpreting his poetry. The Aesculapian poet died at the age of 25. He had spent a greater amount of precious time in his apprenticeship as an apothecary and practicing physician than was allotted to him in the fulfillment of his burning desire to compose metric verse—either that which rhymed or that which conveyed to the reader a new thought, an inspiration, or his elucidation and interpretation of truth. At the age of 20 years Keats wrote,

"O for ten years, that I may overwhelm
Myself in poesy, so I may do the deed
That my own soul has to itself decreed."

Keats became an apprentice apothecary-surgeon at the age of 17 years and acquired practical medical experience in this apprenticeship for four years

After two years of observing, he was permitted to practice as a medical assistant This was followed by the equivalent of an internship at the Borough School of Medicine, an affiliation of Guys and St Thomas hospitals The editor of the *Lancet* for many years, Thomas Wakley, was a fellow novitiate They studied under the intellectual tutelage of Sir Astley Cooper This famous English surgeon was so impressed with Keats that he arranged to have him live with his cousin George Cooper Other attending physicians besides Sir Astley Cooper at Guys Hospital at that time were Richard Bright, Thomas Addison, and Thomas Hodgkins But all was not serious with Keats! On one of the blank pages of a chemistry textbook he wrote,

> Give me woman, wine and snuff
> Until I cry, 'Hold Enough
> You may do so *sans* objection
> Until the Day of Resurrection "

Another classmate was John W Webster, subsequently the professor of chemistry at Harvard College and later murderer of George Parkman, benefactor of Harvard College and donor of the building site for Harvard Medical School (formerly called The Massachusetts Medical College) in 1846

More than five years of medical training and medical practice were sufficient for Keats At the age of 23 he turned from medicine to poetry and permissible passion At least three burning loves of Keats have been described Dante loved his Beatrice, Petrarch his Laura, Keats his Fanny Brawne A portion of deep emotional desires may have been related to his overwhelming illness, pulmonary tuberculosis Other patients afflicted with this malady have experienced an insatiable emotional urge Several of Keats' family died of tuberculosis before Keats succumbed During the last months of his life his money was spent, his love affairs were past history, and, in spite of his multiple adversities, his greatest poem, 'Endymion,' was produced Security need not be a prerequisite for intellectual fecundity

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THE REVELATIONS OF FLEMING

It is generally recognized that, by his work Fleming has saved more lives and perhaps has relieved more suffering than any other man who has ever lived This, by itself, is enough to alter the history of the world This sentiment appears in André Maurois recent biography of Sir Alexander Fleming[1] Maurois begins his grand tour at a remote farm in Scotland where Fleming was born, thence on foot along miles of country road to school at Darvel, to London to live with a brother who advised Alex to go into medicine, thence to St Marys Hospital where he graduated, and in whose tiny (and then) simple laboratory he was to remain the rest of his life, there to discover a substance in a mold that revolutionized the treatment of infectious diseases

Many professors, practitioners, and students previously had seen unwanted molds on their petri dish cultures Many of them had been brought up on farms where they learned to work and observe Nature's ways, as Fleming did, many had spent years at work in laboratories Why did not they discover penicillin? A closer look at the man may suggest an answer

Of many who speak of him in Maurois' book, more speak of Fleming's reticence than of any other quality He lived within an armor of silence and had to be thoroughly known before one could be certain whether he was pleased or annoyed His motto seemed to be "Anything for a Quiet Life' Shyness made him brusque, a quality which mellowed when fame brought him before kings and to other countries throughout the world John Freeman of the team of dedicated workers in Sir Almroth Wright's laboratory said Fleming could "be more eloquently silent than any man I have ever known In the stress of the moment I sometimes called him a blithering idiot, or used some equally opprobrious epithet In reply, Fleming would merely look at me with his barely noticeable Gioconda-like smile, and I think he had the best of the exchange " Sir Henry Dale said when Fleming read a paper on penicillin before the Medical Research Club in 1929 he 'was very shy, and excessively modest,' giving his presentation "in a half-hearted sort of way, shrugging his shoulders as though he were deprecating the importance of what he said All the same the elegance and beauty of his observations made a great impression ' On commencement day in 1945 after Harvard had given him a degree, the president of a distinguished college asked to be introduced to Fleming The president said to Fleming, "I m from Ayrshire, you're from Ayrshire' "Aye,' said Fleming They shook hands and that was all Conversation with him was sometimes difficult His interlocutor would wait for an answer to a question only to get "Hmm, or a groan, or complete silence

Fleming was industrious His colleagues set their watches by the moment of his arrival at the lab, where he spent many evenings and where the amount of work he did was tremendous He never was in a hurry He was not pompous He always tried to see whether anything could be done and never failed to answer hundreds of letters in his own tiny, eloquent, readable hand On a trip abroad, which was especially enjoyed, a friend suggested that he stay longer Fleming replied, 'I have to work for a living' and that, Maurois says, was true In 1912 when he had just returned from camp with the London Scottish regiment, a friend asked how he managed to keep his rifle and boots so spotless in spite of the rain and mud Fleming gave him a "terrifying look" and replied with usual brevity, 'By bloody hard work."

Fleming loved art objects and was an assiduous attendant at auction sales. To join the Chelsea Arts Club, prospects had to paint a picture, and Fleming was ordered to paint a farm scene. He had no training in painting, but he painted a cow, which later was on exhibit. One of two ladies who were discussing his "work" said, "This modern art must mean something, but I confess I cannot make out what it is."

On receiving the Nobel Prize at Stockholm, which he shared with Chain and Florey, Fleming wrote to John Cameron, "after the banquet we adjourned to a student's sing-song and dance. Home at 3 A. M." Next day he dined with the king, "but when we got back to our hotel we adjourned to the bar and drank Swedish beer for a long time."

Even as a father Fleming could be imperturbable. He went fishing in a boat with his son and Dr. Gerold Wilcox. When he hooked a pike, his boy jumped up and fell into the river. Fleming never let go of the rod, leaving it to his guest to fish his son out of the water. He delighted in swimming and gardening. He and Sareen, his first wife, transformed the meadow around their home into a garden of flowers. Clearing the ground took several years. They established green houses, a vine, and "peaches which they trained against a wall." His holidays were short, but he devoted several days each year to running a garden fete for the village.

Of the hundreds of known species of penicillium, many of them elaborate antibiotic substances, but only penicillins have the combination of properties suitable for wide chemotherapeutic use. The one which fell on Fleming's petri dish he thought was the Chrysogenum strain. A mycologist, who happened to be at St. Mary's, said it was Penicillium rubrum. Two years later, Thom, an American mycologist, identified it as P. notatum, a strain closely related to P. chrysogenum. Fleming himself named his antibiotic penicillin, and clinical tests soon proved its therapeutic value. A major problem was to find, among the many, the strain that produced the most penicillin, and the search went on throughout the world. Fleming told his fellow members at the Arts Club, "If any of you chaps has got a pair of mouldy old shoes, I'd very much like to have 'em . . . for something I'm doing at the lab." England's pharmaceutical manufacturers unfortunately at that time were not equipped to produce penicillin on a large scale. Florey and Heatley came to the United States to arrange for mass production, finally reaching the Northern Regional Research Laboratory at Peoria, Ill., where mycologists were still looking for mold-strains which would give a larger yield of penicillin. "Mouldy Mary," a young woman attached to the laboratory, was assigned to buy every variety of mold she could find. One day she came back from the market with a rotten cantaloupe containing a mold of the P. chrysogenum type which was remarkably productive. Maurois says that today most of the strains used, after mutations, come from that Peoria melon.

On a trip to the United States in 1945, Fleming was asked why he had never touched the royalties "which would have enabled you and yours to live as a man should who has rendered such service to humanity." Fleming said, "It never occurred to me," and penicillin, itself, has remained through the years unpatented and free of all royalties.

His death came suddenly at home in his seventy-fourth year. He died as he had lived, quietly, stoically, silently. At the entrance to the farm in Scotland there was placed a tall block of granite to mark his birthplace.

As translated from the French by Gerard Hopkins, Maurois' life of Fleming merits a place among the modern classics in medical biography.

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1. Maurois, A.: The Life of Sir Alexander Fleming, Discoverer of Penicillin, New York, E. P. Dutton & Co., Inc., 1959.

GUIDE FOR EVALUATING CARDIOVASCULAR IMPAIRMENT

To say simply that a patient with cardiovascular disease is permanently impaired does not tell the whole story. The varied degrees of impairment should also be considered. How does cardiovascular disease influence a person's ability to live a normal life? How is the degree of impairment evaluated? Physicians and laymen for years have tried to answer these questions in order that such organizations as the Veterans Administration, insurance companies, the Social Security Administration, workmen's compensation boards, and the courts might render equitable decisions.

The medical profession has a new guide to the evaluation of permanent impairment of the cardiovascular system. This appeared in The Journal March 5, page 1049. In setting up this guide, the A. M. A. Committee on Medical Rating of Physical Impairment established three categories: heart disease, hypertensive vascular disease, and vascular diseases affecting the extremities. Each category is divided into a series of classes, each with its subjective and objective clinical findings and corresponding percentages of impairment of the "whole man." With use of these values, the physician has a practical means for expressing the extent of permanent impairment that will assist lay administrators in pronouncing judgment on permanent disability.

The A. M. A. Committee on Medical Rating of Physical Impairment has now produced three guides. The first one, which dealt with the extremities and back, was published as a special edition of The Journal on February 15, 1958. The second, which was concerned with the visual system, was published as a special article in The Journal, September 27, 1958. In developing these guides the

Committee had the benefit of advice from consultants in the respective fields The guides will be reviewed periodically to insure their continuing value as medical knowledge and techniques advance

While the guides should prove valuable to specialists and members of interested nonmedical groups, they have been prepared with the general practitioner in mind The family doctor is receiving an increasing number of requests from patients to provide a medical evaluation that is to be used in administering the different disability programs This medical evaluation is an appraisal of the nature and extent of the patient's illness or injury as it affects his personal efficiency in the activities of daily living These activities are self-care, communication, normal living postures, ambulation, elevation, traveling, and nonspecialized hand activities

The extent of the physician's responsibility in evaluating the patient's permanent disability should be limited to an evaluation of permanent impairment The evaluation of permanent disability is an administrative appraisal of the patient s present and probable future ability to engage in gainful activity as it is affected by the medical factor, permanent impairment, as well as by such nonmedical factors as age, sex, education and economic and social environment

As the A M A Committee continues its fact-finding work, it will present similar guides concerning other body systems Reprints of the published guides are available on a complimentary basis from A M A headquarters, 535 N Dearborn St, Chicago 10

PRIMARY AMYLOIDOSIS

The deposition of a homogeneous material in various organs of the body was first described in 1824 by Rokitansky Virchow, in 1854, observed that this material stained blue with iodine and sulfuric acid, and termed it 'amyloid," although it has no relation to starch but is a protein usually associated with a sulfate-bearing polysaccharide similar to chondroitin-sulfuric acid Four types of amyloidosis are distinguished primary, secondary, tumor forming, and that associated with myeloma

Recently a certain type of vitreous opacification has been recognized as being due to amyloidosis, thus making it possible to diagnose a systemic disease often undiagnosed during life According to Kaufman,[1] the opacities of the ocular vitreous resemble cotton-wool or glass-wool sheets when seen by the biomicroscope and can provide the necessary clue to the correct diagnosis Kaufman reports on four patients with vitreous opacities due to deposition of amyloid and stresses the familial character of this condition The eyes are not affected in all patients with familial amyloidosis, and it is not established that amyloid vitreous occurs only in the familial type of the disease The vitreous opacities of amyloidosis are typical and may lead to a correct diagnosis, not only in the patient exhibiting it but also in members of the family without ocular manifestations The familial form of primary amyloidosis was first demonstrated by Ostertag in 1950

In 1956, Rukavina and his co-workers reported on a family in which one-half of the cases with familial amyloidosis had an abnormal or poorly resolved alpha-2 globulin in the serum as studied by free electrophoresis

Several theories exist as to the origin of amyloidosis The fact that animals, especially horses, used in the preparation of antisera frequently show amyloidosis has led to the belief that amyloid is the product of antigen-antibody reaction Thomas defines amyloid as an extracellular homogeneous hyaline substance which stains metachromatically with methyl violet In secondary amyloidosis deposits are found in the liver, spleen, kidneys, and adrenals In primary amyloidosis this substance may be found in any tissue or organ but is most frequently seen in the heart, blood vessels, and other mesothermal structures

The etiology of primary amyloidosis is more obscure than that of secondary amyloidosis The latter is seen in association with chronic tuberculosis of lungs, bones, and joints, chronic pyogenic osteomyelitis, syphilis, certain tumors, chronic nephritis, liver cirrhosis, and rheumatoid arthritis Deposits in primary amyloidosis may be seen in the larynx, tongue, trachea, bronchi, skeletal muscles, joints, bones, and the media of the arteries When amyloid is stained by metachromatic aniline dyes, such as methyl violet or methyl green, the amyloid is stained red and the tissues the color of the dye Congo red has an affinity for amyloid, and its disappearance from the blood after intravenous injection is used as a clinical test The amyloid deposits can produce by pressure upon surrounding cells degenerative processes such as cloudy swelling, atrophy, or necrosis Warren and Reimann advanced the theory that a primary local defect of mesenchymal tissue or of fibroblasts resulted in the formation of amyloid The Congo red injection test is not conclusive in the diagnosis of amyloid disease Biopsy is the most helpful diagnostic method, the skin, gingiva, and liver are preferred The presence of an abnormal serum alpha-2 globulin is suggestive The appearance of amyloid vitreous seems to be diagnostic and occurs only in the familial type

The neurological changes in the two patients of Kaufman are interpreted by Haase[1] as being caused by deposition of amyloid material in the peripheral nerves, the dorsal root ganglions, and the meninges Diarrhea, constipation, sphincteric disturbances, or impotence suggest involvement of the autonomic nervous system

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[1] Primary Amyloidosis Clinical Staff Conference at the National Institutes of Health Ann Int Med 52 668 (March) 1960

E Vincent Askey, M D, President, American Medical Association

No Physician Can Shun Role In Political Life

"THE plain truth is that men are tired of liberty," said Mussolini in March, 1923

The events of July, 1960, in the United States have demonstrated to the world that Americans, however, are not tired of liberty but are energetic about liberty and self-government For one month, at least, they have shown their strong will and keen sense of responsibility for the best form of government yet devised by man

Through the first few days of November this same zeal undoubtedly will be in evidence throughout the land What happens thereafter is almost as certain as the night following the day Americans doctors emphatically included, will slide neatly and conveniently back into their own "fat, dumb and happy complacency," as Arthur H Motley, president of Parade Publications, Inc, has put it so aptly

During the furor of a presidential election most of us become sufficiently interested in candidates, nominees, and almost all aspects of self-government Immediately following the election disinterest in politics prevails, and the citizenry falls into a pattern of reacting rather than acting

Within our own profession can we maintain the same zeal for public affairs that exists in this pre-election period? Or will we too drift back, "tiring" of freedom to act and freedom to participate in self-government?

I hope that our experience in the political field in the last few years, especially with the U S Congress, will be enough to spur us on to further action at the local, state and national levels

At the local level I can bear witness that no job in public affairs is unimportant, whether it is an elected post on a school board or an appointive job on a community committee And I can further testify that political performance cannot be purchased It must come from interested and willing citizens, for only manpower plus brainpower really does the job thoroughly

Physicians can be proud that 361 members of the medical profession have served in Congress since the First Continental Congress We can be proud that scores of physicians were delegates to the recent national political conventions in Los Angeles and Chicago We can be proud that four physicians are running for Congress for the first time this year —Fred Obley of Elwood City in Pennsylvania's 25th district, Durward G Hall of Springfield in Missouri's Seventh District, Floyd M Burgeson of Des Moines in Iowa's Fifth District, and Edwin C Durno of Eugene in Oregon's Fourth District

No trade or profession has a monopoly on good candidates for political office, and no man or woman should be barred from seeking office because he is in a profession of service

Politics demands that the participant be practical, and the physician certainly is a practical man It deals with particular problems, and the physician faces such issues daily It involves study and probing, and the physician is an expert at diagnosis It requires foresight, and the physician in his practice certainly must have imagination and ideas to prevent future problems And it calls for decisive actions to alleviate or solve dilemmas, and here again the physician has experience in treatment and rehabilitation

Finally, politics calls upon the participant to grow—to learn and to progress What physician can fail to grow—keep abreast and ahead of the times?

Let each of us pledge himself now to full participation in our government Let none of us ever tire of liberty

E. Vincent Askey M.D.

MEDICAL NEWS

BODY OF KIDNAPED DOCTOR FOUND

Dubuque Physician Missing Ten Days.—The body of Dr Edward R Bartels, Dubuque, Iowa, was found in a wooded area about five miles west of Galena, Ill, on July 21, 10 days after the physician's disappearance The Federal Bureau of Investigation announced that charges of kidnaping were brought against a 25-year-old former convict from Michigan who was arrested in Birmingham, Ala, while trying to sell Dr Bartels' car

Dr Edward R Bartels

Dr Bartels, a 1953 graduate of the State University of Iowa College of Medicine, Iowa City, left his home the evening of July 11 after receiving a call to treat a woman who was "critically ill" Later, Mrs Bartels received a call from a man saying that Dr Bartels was "calling in a specialist" and would not be home that night When the physician did not return the following day, police were notified

The Dubuque County Medical Society offered a reward for information on Dr Bartels' disappearance

CALIFORNIA

Dr Aldes Wins Presidential Award.—Dr John H Aldes, Los Angeles, has been named to receive the physician's award for 1959 by the President's Committee on Employment of the Physically Handicapped Dr Aldes, an orthopedic surgeon, is director of the rehabilitation department of the Cedars of Lebanon Hospital in Los Angeles The award, an illuminated scroll signed by the President, is in recognition of Dr Aldes' contribution to the committee's program of "achieving equality of opportunity in employment for the physically handicapped" It will be awarded at the annual banquet of the Congress of Industrial Health of the A M A in Charlotte, N C, Oct 11

CONNECTICUT

Associate Deans Named at Yale.—The promotion of Thomas R Forbes, Ph D, and Dr Arthur Ebbert Jr to the rank of associate deans at the Yale School of Medicine was announced July 10 Both men have been serving as assistant deans Dr Forbes, who is also associate professor of anatomy, has been on the Yale faculty since 1945 He has been assistant dean since 1948 and chairman of the Committee on Admissions Dr Ebbert received his undergraduate and medical training at the University of Virginia, and was instructor in medicine and assistant to the dean at the University of Virginia School of Medicine in 1952-1953 He came to Yale in 1953 as instructor in medicine and assistant dean and was promoted to assistant professor in 1954 He has been in charge of postgraduate medical education and director of the Yale Diagnostic Clinic

NEW HAMPSHIRE

Convocation to Consider Moral Issues in Medicine.—"The Great Issues of Conscience in Modern Medicine" will be discussed at Dartmouth College, Hanover, Sept 8-10, under the sponsorship of the college and the medical school The purpose of the three-day academic convocation is to "further discussion of the new moral questions that have arisen from achievements of modern science relating to medicine," including the population explosion," by-products of research such as radioactive material, and the possible extension of preventive medicine to mental illness Problems will be discussed in speaking sessions and panel discussions in which medical and physical scientists and philosophers are being invited to participate Dr Rene

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Physicians are invited to send to this department items of news of general interest for example those relating to society activities new hospitals, education and public health Programs should be received at least three weeks before the date of meeting

Jules Dubos, member and professor of the Rockefeller Institute in New York and an editor of the *Journal of Experimental Medicine,* has been named chairman of the convocation Participants will include novelist Aldous Huxley, George B Kistiakowsky, special assistant to President Eisenhower for Science and Technology, and Dr Brock Chisholm, Toronto, Canada, former director general of the United Nations' World Health Organization

NEW YORK

J. N Adam Memorial Hospital Converted for Mentally Retarded Patients —The J N Adam Memorial Hospital, Perrysburg, is being renovated from a facility for tuberculous patients to one for the mentally retarded, Dr Arthur W Pense, deputy commissioner in charge of the Office of Mental Retardation of the New York State Department of Mental Hygiene, announced The remodeled hospital will be known as the J N Adam State School Division of Gowanda State Hospital and will be utilized for the treatment of severely retarded children requiring bed care

Report on Poliomyelitis —The State Health Department announced July 5 that 25 cases of poliomyelitis, 21 of them paralytic, were reported in New York State, exclusive of New York City, during the first six months of 1960 Six deaths from poliomyelitis were reported during the first half of the year None of the deaths occurred in persons having three or more injections of the Salk vaccine During the first half of 1959, 31 cases of poliomyelitis, 24 of them paralytic, were reported An average of 127 cases, 80 of them paralytic, occurred during the same period in each of the years 1951 through 1953 Four of the cases of paralytic poliomyelitis reported this year occurred in persons who received no vaccine

Dr Dobkin to Head New Anesthesiology Department —Effective Sept 1, Dr Allen B Dobkin will be head of the department of anesthesiology, State University of New York College of Medicine, Syracuse Dr Dobkin's appointment is concurrent with the formation of the department of anesthesiology at the Medical College, anesthesiology was formerly affiliated with the department of surgery The departmental office will be located in the University Hospital until the new Teaching and Research Hospital is built Dr Dobkin comes to the Medical College from the University of Saskatchewan College of Medicine, Saskatoon, Canada, where, since 1955, he has held the positions of assistant professor and associate professor in anesthesia He received his M D degree from the University of Toronto Faculty of Medicine

Personal —The provisional appointment of Dr George M Warner as director of the State Bureau of Chronic Disease and Geriatrics was announced June 9 by Dr Herman E Hilleboe, state health commissioner Dr Warner, home care executive and deputy chief, Division of Social Medicine, Montefiore Hospital, Bronx, since 1955, succeeds Dr Frank W Reynolds, who resigned in September, 1959, to become associate professor of public health practice at the University of Michigan —Dr I Jay Brightman, Albany, was appointed assistant commissioner for Chronic Disease Services of the State Health Department Dr Brightman joined the staff of the State Health Department in 1941, and in 1956 he was appointed executive director of the Interdepartmental Health Resources Board He is a member of the A M A's Committee on Indigent Care and a past-chairman, medical care section, American Public Welfare Association —Dr Edward R Schlesinger, Albany, was appointed assistant commissioner for Special Health Services in the State Health Department Dr Schlesinger joined the State Health Department as an assistant district health officer in 1941

New York City

Dr Failla Retires —Gioacchino Failla, D Sc, professor of radiology, Columbia University College of Physicians and Surgeons, retired from the Columbia faculty June 30 In recognition of his work, Dr Failla was designated professor emeritus of radiology by Columbia's trustees, effective July 1 Dr Failla became interested in the biological and medical applications of radium and x-rays in 1916 while he was a graduate student in physics at Columbia and held a part-time position at Memorial Hospital in New York City After becoming attending physicist at Memorial Hospital, Dr Failla worked with the Atomic Energy Commission, where he was the first chairman of the Advisory Committee on Isotope Distribution and later chairman of the Advisory Committee on Biology and Medicine

New Department Heads at Columbia —Chairmen of the departments of pediatrics and pathology at Columbia University's College of Physicians and Surgeons have been appointed Dr Edward C Curnen Jr, professor of pediatrics and chairman of the department of pediatrics of the University of North Carolina School of Medicine, Chapel Hill, has been appointed chairman of the department of pediatrics and Carpentier Professor of Pediatrics Dr Donald G McKay, assistant professor of pathology, Harvard Medical School, Boston, has been named chairman of the department of pathology and Delafield Professor of Pathology Dr Curnen, who succeeds Dr Rustin McIntosh, also will be attending pediatrician and director of pediatric service at Babies (Presbyterian) Hospital at the Columbia-Presbyterian Medical Center Dr McKay, who succeeds Dr. Harry P Smith, will be attending pathologist and director of pathology service at the hospital Dr Curnen received his M D degree at Harvard in 1935 He has taught at the Yale University School of Medicine and at Harvard Medical School Dr McKay received his M D in 1945 from the University of California He has been associated with Harvard Medical School since 1948, when he became an instructor Before joining the Harvard faculty, Dr McKay taught at Boston University School of Medicine and at Tufts Medical School

NORTH CAROLINA

Study Air Pollution —Results of a recent nine month's study of air pollution in North Carolina made by the State Board of Health in conjunction with the U S Public Health Service have been released in booklet form by Dr J W R Norton, state health director The study included tests of air samples across the state and a review of the legislation Smoke, soot, or fly-ash from fuel-burning equipment in commercial, industrial, or municipal establishments were cited as the major contributing factors in air pollution, but wood industries, asphalt paving material plants, pulp and paper mills, open dumps, and poorly operated or maintained sewage disposal systems were found to be at fault as well The report recommended that legislation, which now limits control of air pollution to the jurisdiction of a few cities, be extended

PENNSYLVANIA

St Francis Opens New Wing —The South Wing of St Francis General Hospital and Rehabilitation Institute, Pittsburgh, completed earlier this year at a cost of 7 million dollars, will provide an additional 300 beds, plus 11 operating rooms and a new pediatric department The Rehabilitation Institute will be able to take care of 42 inpatients and 75 outpatients, and it includes a gymnasium and other facilities for occupational, physical, speech, and hearing therapy Heading the institute will be Dr J Huber Wagner, former chief surgeon of United States Steel, and medical director is Dr Thomas C Hohmann

Philadelphia

Graduate Receives Memorial Award —The Beatrice Sterling Hollander Memorial Prize was awarded to Dr Phyllis Colacicco Marciano, a member of the 1960 graduating class at Woman's Medical College of Pennsylvania A fund was established in Dr Hollander's memory by her family and friends on her death in December, 1958 She had received her medical degree at Woman's Medical College in 1941, and the prize is designated for the 'Student in the Graduating Class Who Shows Promise of Leadership, High Character and Creativeness in Her Profession' Dr Marciano is one of the "honor" members of the 1960 class at Woman's Medical College, receiving her medical degree "cum laude"

TEXAS

New Editor Appointed for State Journal —Miss Ruth Trahan, formerly an assistant editor for the M D Anderson Hospital and Tumor Institute in Houston, is the new managing editor for the *Texas State Journal of Medicine* Miss Trahan fills the position formerly held by the late Miss Harriet Cunningham Prior to receiving her bachelor of journalism degree from the University of Texas, Miss Trahan had served as a lieutenant in the Nurse Corps, U S Naval Reserve She is a graduate of the St Joseph's School of Nursing in Houston Miss Trahan was an editorial assistant for the *Texas State Journal of Medicine* for four years before becoming an associate editor with the Medical Arts Publishing Foundation in Houston, and then going to her present position

WISCONSIN

Training Program in Endocrinology —The University of Wisconsin Graduate School at Madison announced a postdoctoral training program in endocrinology beginning July 1 Its purpose is to 'increase the qualified personnel for teaching and carrying on research in endocrinology Breadth of training will be emphasized It will consist of an integrated program of laboratory research, seminars, colloquiums, workshops, and teaching under the coordinated auspices of faculty members from the colleges of Letters and Science, Medicine, and Agriculture Candidates for postdoctoral fellowships (M D or Ph D) will be selected on the basis of professional promise and career interest' Appointments will carry a yearly stipend of $6,500 Applicants may apply to William H McShan, Ph D , Birge Hall, University of Wisconsin, Madison 6, Wis

GENERAL

Heart Group Establishes Department of Services —The establishment of a new department of services to affiliates by the American Heart Association, 'to expand and strengthen its assistance to state and local Heart Associations in developing their programs,' was announced by Mr Rome A Betts, executive director of the association The new department will coordinate the association's fund-raising and public information programs, field consultation services, and assistance to local heart associations in recruiting and training personnel

Urology Award Offered —The American Urological Association is offering an annual award (first prize of $500, second prize $300, and third prize $200) for essays on the results of some clinical or laboratory research in urology Competition is open to urologists who have been graduated not more than 10 years, and to interns and residents doing research in urology The first prize essay will be presented at the May 22-25, 1961, meeting of the association in Los Angeles For information, write the Executive Secretary, Mr William P Didusch, 1120 N Charles St, Baltimore Essays must be submitted before Dec 1

Report on Hospital Construction.—The American Association of Fund-Raising Counsel, Inc, reporting on construction gains for the first five months of 1960, announced that private hospital construction was 236 million dollars, a 4% increase The association indicated that hospital construction may total 675 million dollars this year, "possibly making 1960 the greatest growth year in a decade" An estimated 300 million dollars of total construction costs may be expected to come from private sources The AAFRC is a nonprofit organization of 31 major fund-raising firms specializing in counseling, directing, and organizing fund-raising activites in the U S and Canada

Radiology Meeting in Denver—The Rocky Mountain Radiology Society will hold its annual meeting in Denver Aug 11-13 Guest speakers for the meeting include Dr Ted F Leigh, department of radiology, Emory University Clinic, Atlanta, Ga, Dr Charles R Perryman, director, department of radiology, Mercy Hospital, Pittsburgh, Dr Sydney F Thomas, Palo Alto Medical Clinic, Palo Alto, Calif, Dr Benjamin Felson, professor of radiology, Cincinnati University, and Dr David M Gould, professor of radiology, University of Colorado, Denver For information, write Dr John H Freed, 4200 E Ninth Ave, Denver 20, Secretary-Treasurer

Inaugural Meeting Held for Tropical Dermatology Group—The inaugural meeting of the International Society of Tropical Dermatology was held on May 10 at the Rockefeller Institute, New York City "Elephantiasis Tropica and Elephantiasis Nostra" was the topic of the presidential address by Prof Aldo Castellani The secretary-general, Dr Frederick S Reiss, delivered an address informing the members that 50 countries are represented in this organization with almost 1,300 charter members The date and place of the first international congress were discussed, and either 1962 or 1963 was considered likely, in Mexico City or Rio de Janeiro A reception was given at the institute For information, write Dr Reiss at 870 Fifth Ave, New York 21

Anesthesiologists Dedicate Headquarters Building—Dedication services of the headquarters building of the American Society of Anesthesiologists were held at the building site in Park Ridge, Ill, May 21 Dr Leo V Hand, president, presided at the services, and the dedicatory address was presented by Dr Leonard W Larson, of Bismarck, N D, the new President-Elect of the American Medical Association, titled, "These Are Your Monuments" The building was built under the direction and supervision of the society's Committee on Building Fund, the members of which were Dr Albert M Betcher, New York City, J Earl Remlinger Jr, Wilmette, Ill, and Daniel C Moore, chairman, Seattle The address of the new building is 515 Busse Highway, Park Ridge, Ill

Conference on Research in Biology and Engineering—Researchers in the new science of bionics (biology and engineering) will discuss their work at a symposium Sept 13-15, sponsored by the Air Force's Air Research and Development Command, Wright Air Development Division, Wright-Patterson Air Force Base, Ohio Bionics is described as "the art of applying knowledge of biological systems and techniques to the solution of engineering design problems" The current objective is to apply principles discovered in the study of biological system to engineering design Persons interested in attending the symposium should communicate with the Commander, Wright Air Development Division, Attn WWRDA, Major J E Steele, Wright-Patterson Air Force Base, Ohio

Project HOPE Physician Leaves for Indonesia—On July 1, Dr Mark S Beaubien, vice-president of medical operations for Project HOPE, left San Francisco for Djakarta, Indonesia Project HOPE, a privately sponsored program to share U S medical knowledge and skills with newly developing countries, will send a floating medical training center to Southeast Asia during its first year of operation The permanent staff of the S S Hope will include 15 physicians, 2 dentists, 25 nurses, and 30 auxiliary personnel During the months remaining before the arrival of the S S Hope in Indonesia, Dr Beaubien will work with the Ministry of Health and representatives of the Indonesian medical professions in developing a medical training program and an itinerary for the ship

Meeting of Record Librarians—The 32nd annual meeting of the American Association of Medical Record Librarians will be held at the Olympic Hotel, Seattle, Oct 10-13 Increasing hospital efficiency by streamlining procedures will receive major attention as members hear how future hospital planning will affect medical records and how medical record departments may be streamlined to keep pace Dr Hugh C MacGuire, Atomedic Research Center, Montgomery, Ala, will be among the principal speakers Education, research, and changing concepts in patient care will be discussed by educators and physicians A report on the third International Congress on Medical Records, held in Edinburgh, Scotland, in April, will be presented

For information, write the American Association of Medical Record Librarians, 840 N Lake Shore Dr, Chicago 11

Ambulance Operators Form International Society—Meeting in Chicago, ambulance operators from all over the United States and Canada organized the International Society of Professional Ambulance Services Membership is to be by invitation only Objectives of the new organization include the following to advance the science and art of ambulance service, to provide better transportation and protection of the sick, injured, and infirm, to exchange information on improved ambulance services for the public and the medical profession, to advance the profession of ambulance service through institutes, meetings, publication, etc, to aid in the technical advance of ambulance equipment, and to facilitate cooperation between professional ambulance services, the medical profession, hospitals, municipalities, civil defense organizations, and all others interested in improved ambulance service Headquarters for the new society will be at 332 S Michigan Ave, Chicago

Medical Prize Offered by Italian Academy—The Medical Academy of Turin, Italy, announced a competition for the third Saint Vincent Prize for Medical Sciences The 10,000,000-lire prize was established by the "Regione Valle d'Aosta' and "Società Incremento Turistico Alberghiero Valdostano' of Saint Vincent 'to favor the development of medical research" To be eligible, a candidate must be proposed before Oct 31 by at least 10 members of the academy, by the medical faculty of an Italian University, by the winners of the St Vincent Prize, or by the 'Accademia dei Lincei" and by "presidents of the foreign medical academies and faculties' The winner will be announced in June, 1961, at the fourth International Medical Meetings in Turin The first winner of the award in 1954 was Prof Selman A Waksmann, Rutgers University, New Jersey, for the discovery of streptomycin For information, write Dr Prof Angelo Allodi, Secretary General, 18, Via Po, Turin, Italy

Pediatric Fellowships Awarded—The recipients of the 1960 Wyeth Laboratories pediatric residency fellowships were announced July 5 by Dr Philip S Barba, Philadelphia, past-president of the American Academy of Pediatrics and chairman of the fellowship selection committee The pediatric program, sponsored by the Wyeth Fund for Postgraduate Medical Education, provides a grant of $4,800 to each physician, enabling him to spend two years of advanced study in the care and treatment of children The recipients, from 16 different states, are the third group to benefit from the program established in 1958 by the Philadelphia pharmaceutical manufacturing company Selection was made on the basis of 'interest in pediatrics, character, able performance of duties, and academic competence" The Wyeth fellowship winners may attend any hospital whose residency is accredited by the Residency Review Committee composed of representatives from the American Board of Pediatrics, the American Academy of Pediatrics, and the Council on Medical Education and Hospitals of the American Medical Association

Prevalence of Poliomyelitis—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated

	July 2 1960		July 4 1959
Area	Paralytic Type	Total Cases	Total
New England States			
Maine			
New Hampshire			
Vermont			
Massachusetts		1	
Rhode Island	8	10	
Connecticut			
Middle Atlantic States			
New York	1	1	4
New Jersey			1
Pennsylvania			
East North Central States			
Ohio			3
Indiana		1	1
Illinois	8	4	
Michigan			6
Wisconsin			1
West North Central States			
Minnesota	1	1	
Iowa			38
Missouri			16
North Dakota			
South Dakota			
Nebraska			11
Kansas			3
South Atlantic States			
Delaware			
Maryland			
District of Columbia			
Virginia			2
West Virginia	2	2	
North Carolina		1	
South Carolina			1
Georgia			10
Florida			3
East South Central States			
Kentucky			1
Tennessee			3
Alabama			5
Mississippi	1	1	6
West South Central States			
Arkansas	1	2	6
Louisiana	3	3	8
Oklahoma			7
Texas	2	8	10
Mountain States			
Montana			
Idaho			
Wyoming			1
Colorado	1	1	1
New Mexico			4
Arizona			1
Utah			
Nevada			
Pacific States			
Washington			1
Oregon			2
California	[illegible]	18	9
Alaska			
Hawaii			
Territories and Possessions			
Puerto Rico	21	24	
Total	[illegible]	[illegible]	[illegible]

Technical Assistant Needed by World Health Organization—The World Health Organization announced a vacancy for the post of Technical Assistant," a person with a college degree and some academic and editorial experience in the biological sciences The technical assistant will review technical literature on viruses, select references and make summaries for the preparation of articles or documents, keep biographical references up to date, and assist in the preparation of conferences, expert committees, and other group meetings As much of the work will be editorial, proficiency in English should be high, a working knowledge of other languages—especially French—is "highly desirable" This post is classified in the professional category and carries a basic salary of $3,600, plus a cost of living allowance and other emoluments The salary and allowances are tax-free There is provision for Home Leave, with transportation to the home country paid by the organization, every second year For information and application, write Dr A C Saenz, Medical Officer, Virus Diseases, Division of Communicable Diseases, World Health Organization, Palais des Nations, Geneva, Switzerland

Congress on Rehabilitation in New York City—The eighth World Congress of the International Society for the Welfare of Cripples will be held in New York City, Aug 28 to Sept 2, with the National Society for Crippled Children and Adults as host society Speakers from nearly 50 nations will appear on the congress program, emphasizing help to the crippled as a means for fostering international cooperation General session topics, such as "Progress and Needs in Rehabilitation," "Organizing to Meet the Challenge of Crippling Disease," "The Contribution of the Handicapped to the World Economy," and "The Contribution of the Handicapped to World Understanding," will be expanded through 15 major section meetings, 10 special sessions, and a series of informal discussion groups Three sessions will feature presentation of selected papers, and another will be a forum for students from foreign countries who are studying rehabilitation in the United States Secretary of State Christian A Herter and Mayor of New York Robert Wagner will deliver opening addresses, Dr Howard A Rusk, New York City, will give the keynote address Among the activities planned are exhibits, a film theater, field trips, a banquet, and postsession tours Registration is open to all persons who wish to attend For information, write The Eighth World Congress Office, 2023 W Ogden Ave, Chicago 12

Medical Writers to Meet in Chicago—The 17th annual meeting of the American Medical Writers' Association will be held at the Hotel Morrison, Chicago, Sept 30-Oct 1 Dr Austin Smith, president, Pharmaceutical Manufacturers Association, Washington, D C, and former editor of THE JOURNAL, will preside Papers on various phases of medical writing will comprise the all-day program Sept 30 It will be climaxed with a fellowship hour, sponsored by the Schering Corporation, and a banquet The program Oct 1 will feature morning and afternoon sessions titled "Conference on Medical Communications," arranged by Dr William D Snively Jr, Evansville, Ind., medical director, Mead Johnson Co Dr Walter Kahoe, director, medical department, J B Lippincott Co, will preside at the morning session, which will be devoted to the publishing and editing aspects of medical writing Dr Justus J Schifferes, director, Health Education Council, will preside at the afternoon session, which will be devoted to the technique of medical writing A complete program of the meeting may be obtained from Dr Harold Swanberg, Secretary, AMWA, W C U Bldg, Quincy, Ill Persons interested in any phase of medical communications are invited There is no registration fee for the Sept 30 sessions Nonmembers pay a $5 registration fee for the Conference on Medical Communications, Oct 1

Heart Association to Meet in St Louis—The American Heart Association's 33rd annual scientific meeting, to be held in Kiel Auditorium, St Louis, Oct 21-23, will present six sessions of clinical interest, to run concurrently with the investigative scientific programs, stressing the application of findings in cardiovascular research These sessions, to include symposiums, panels, lectures of general interest, and papers on results of research, are acceptable for category II credit by the American Academy of General Practice The opening session will include introductory remarks by Dr A Carlton Ernstene, Cleveland, president of the American Heart Association, and the Lewis A Conner Memorial Lecture, "Physiology of the Circulation as Viewed by the Internist," by Dr Eugene A Stead Jr, chairman, department of medicine, Duke University School of Medicine The remainder of the session will be conducted jointly by the AHA Council on Clinical Cardiology and the American College of Cardiology The association's Albert Lasker Award and the George E Brown Memorial Lecture, "Clinical Physiology of the Splanchnic Circulation," will be given by Dr Stanley E Bradley, chairman, department of medicine, Columbia University College of Physicians and Surgeons Sessions on Oct 23 include three symposiums "Complete Heart Block," "Nondietary Factors in Coronary Artery Disease," and "Lipids and Arteriosclerosis" Films and scientific and industrial exhibits are planned For information, write the American Heart Association, 44 E 23rd St, New York 10

FOREIGN

International Meeting on Electromyography—Sponsored by the World Federation of Neurology and the French E E G Society, an International Meeting on Electromyography will be held at the neurological department of the Strasbourg Faculty of Medicine, France (Director Prof F Thiebaut) Oct 17-20 This meeting is designed for all physi cians who are seeking electromyography initiation and for those who have done personal research work in this field After the meeting, participants will be able to follow a practical course for one week For information, write Dr F Isch, Laboratoire d Electromyographie, Clinique Neurologique, Hospices Civils, Strasbourg, France This meeting will follow the European Electroencephalographic Information Meeting, to be held in Marseille, France, Oct 12-15

CORRECTION

Smallpox Vaccination—In The Journal May 14 page 199, in the letter from Germany entitled "Smallpox Vaccination," it was stated that "in Munich only 1% of the children coming for revaccination had fraudulent vaccination certificates" The ratio was 1 per 1,000, not 1 per 100

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology *Written* Various locations, June 30 Sec, Dr Forrest E Leffingwell, 217 Farmington Ave, Hartford 5, Conn

American Board of Dermatology Final date for filing applications of candidates completing training by October 15, 1960 is March 1, 1961 *Written* Several cities, June 5 1961 *Oral* Philadelphia, Oct 13-16, 1961 Sec, Dr Maurice J Costello, One Haven Avenue, New York 32, New York

American Board of Internal Medicine New York City, Nov 14-17 Closing date for filing application was July 1 *Written* Oct 17 Closing date for filing application was May 1 Schedule for 1961 *Written Examination*, October 16 *Oral Examinations* New Orleans, Jan 30-Feb 2, Chicago, April 4-7, Los Angeles, Sept 26-29, New York City, Nov 7-10 Closing date for acceptance of applications for the January and April examinations is October 1, 1960, and for the September and November examinations is June 1, 1961 Sec-Treas, Dr William A Werrell, One West Main St, Madison 3, Wis

American Board of Neurological Surgery *Oral* New Haven, Nov 13-16 Final date for filing application is Sept 1 Sec, Dr Donald D Matson, 300 Longwood Ave Boston 15

American Board of Obstetrics and Gynecology *Written* Various cities of the United States, Canada, and military centers outside of continental United States, January 13 *Oral* Chicago, Apr 7-14 Application for certification, new and reopened in Part I, and requests for reexamination in Part II are now being accepted Deadline for receipt of applications for the written examination is August 1 Candidates submitting applications in 1960 for the 1961 examinations are not required to submit case reports as previously required to complete the Part I examination In lieu of this requirement, new candidates are required to keep in their files a duplicate list of hospital admissions as submitted with their application, for submittal at the annual meeting in Chicago should they become eligible to take the Part II (oral) examination Reopened candidates will be required to submit case reports for review thirty days after notification of eligibility Exec Sec, Dr Robert L Faulkner, 2105 Adelbert Road, Cleveland 6

American Board of Ophthalmology *Written* Jan 23, 1961 Deadline for filing applications was July 1 *Oral* Chicago, Oct 3-7 Sec, Dr Merrill J King, Box 236 Cape Cottage Branch, Portland, Maine

American Board of Orthopaedic Surgery *Written, Part I* Palo Alto, Calif, Nashville, Tenn, Philadelphia, June 19-20 Final date for filing application is Nov 30 *Oral, Part II* Miami Beach, Jan 4-6 Final date for filing application was July 1 Sec, Dr Sam W Banks, 29 E Madison St, Chicago 2

American Board of Otolaryngology *Oral* Chicago, Oct 3-6 Final date for filing application was April 1 Sec, Dr Dean M Lierle, University Hospitals, Iowa City

American Board of Pathology *Examination* Indianapolis, Oct 20-22 Final date for filing application is Sept 15 Sec, Dr Edward B Smith, 1100 W Michigan St, Indianapolis 7

American Board of Pathology *Examination Special Field of Forensic Pathology* New Orleans, Nov 13 Final date for filing application is Oct 1 Sec, Dr Edward B Smith, 1100 W Michigan St, Indianapolis 7

American Board of Pediatrics *Oral* Chicago, Oct 21-23 Final date for filing application has passed *Written* New York City, January Final date for filing application is Dec 1 Sec, Dr John McK Mitchell, 6 Cushman Road, Rosemont, Pa

American Board of Plastic Surgery Entire examination—*written*, and *oral* and *practical* given in May of each year Final date for submitting case reports is November 1 Next examination to be given in New York City, May 1961 Corres Sec, Mrs Estelle E Hillerich, 4647 Pershing Ave, St Louis 8, Mo

American Board of Proctology *Oral and Written, Parts I and III* Philadelphia, Sept 24 Final date for filing application was June 30 Sec, Dr Stuart T Ross, 520 Franklin Ave, Garden City, N Y

American Board of Psychiatry and Neurology New York New York, Dec 12-13, New Orleans, Mar 20 21, and Chicago, Oct 9-10, 1961 Sec, David A Boyd, Jr, 102-110 Second Ave, S W, Rochester, Minn

American Board of Radiology *Examination* Cincinnati, Dec 10 13 Deadline for filing applications for the June examination was Jan 1 Filing deadline for the December examination was July 1 A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications Sec, Dr H Dabney Kerr, Kahler Hotel Bldg, Rochester, Minn

American Board of Surgery *Written* (Part 1), Various Centers, Dec 7 *Candidates are urged to apply several months before completion of training requirements* The closing date for filing applications is August 1 Those completing training requirements after September 30 cannot be considered for the December Part I examination of the same year *Oral* (Part II)—New Haven, Sept 26-27, Indianapolis, Oct 24 25, Buffalo, Nov 14-16, Nashville, Dec 12-13, Philadelphia, Jan 16-17, Houston, Feb 13-14 Columbus, Ohio, Mar 13-14, New York City, April 19-20, Portland, Ore, May 15-16, San Francisco, May 18 19 No examinations will be held in June, July or August Sec-Treas, Dr John B Flick, 1617 Pennsylvania Blvd, Philadelphia 3

Board of Thoracic Surgery *Written* Various centers throughout the country, Sept 9 Final date for filing application was July 1 *Oral* Oct 1960 Final date for filing application is July 1 Sec, Dr Wm M Tuttle, 1151 Taylor Ave, Detroit 2

American Board of Urology *Written* December *Oral-Clinical* Chicago, February 1961 Exec Sec Mrs Ruby L Griggs, 30 Westwood Road Minneapolis 26

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

Personal.—Dr Benjamin B Wells, director of medical education service for the Veterans Administration in Washington, D C, was appointed the VA's assistant chief medical director for research and education in medicine He succeeds Dr John B Barnwell, who retired in March

PUBLIC HEALTH SERVICE

Change in Quarantine.—Two actions designed to expedite the arrival of travelers from abroad have been approved

1 Travelers arriving in the United States from Jamaica, who have not gone elsewhere during the previous two weeks, are no longer required to show proof of smallpox vaccination This exemption is based on the Public Health Service's policy of removing quarantine restrictions whenever possible without weakening essential safeguards against the bringing in of communicable disease Other quarantine-exempt areas are Canada, Iceland, Greenland, the Canal Zone, the west coast of lower California, and the following islands Bahamas, Bermudas, British Virgin Islands, Cuba, Aruba, Curaçao, St Pierre, and Miquelon

2 Planes arriving here from northern Europe are no longer required to have routine spraying with insecticide Planes from all other parts of the world arriving at airports in the northern United States are no longer required to be sprayed between Oct 1 and March 31 At airports in South Carolina, the Gulf states, and along the Mexican border, however, spraying will be continued the year round The purpose of insecticide spraying is to prevent the introduction of such insect-borne diseases as yellow fever, malaria, and typhus For this reason the Public Health Service will continue to require spraying, at all United States airports, for any plane arriving from an area of the world where one of these diseases, or any other insect-borne disease, is reported Approved insecticides must be used

Personal.—Dr Harry A Sauberli was named medical officer in charge of the Indian Health Area office at Portland, Ore Dr Sauberli will administer health and medical care services for an estimated 26,000 Indians in Oregon, Washington, and Idaho He has been assistant area medical officer of the Portland area since 1958, and will succeed Dr Robert L Zobel, who became medical officer in charge of the service's Indian Health Area office at Albuquerque, N M

Personal.—Douglas H K Lee, M D, has been appointed chief of the research headquarters of the Occupational Health Program at Cincinnati He and field studies of occupational health problems will be responsible for directing technical research and professional and technical consultation services to state agencies, labor, and industry

NATIONAL ACADEMY OF SCIENCES–NATIONAL RESEARCH COUNCIL

Food and Drug Review Committee.—A special committee was appointed to review the policies, procedures, and decisions of two divisions of the Food and Drug Administration These are the division of antibiotics, of which Dr Henry Welch was formerly the chief, and the new drug division of the bureau of medicine The committee has been assigned for administrative purposes to the division of medical sciences of the Academy-Research Council The findings will be reported to Secretary Flemming by Dr Detlov W Bronk

The committee will be headed by Dr C Phillip Miller, Professor of Medicine, Department of Medicine, University of Chicago Other members are Drs John H Dingle, Professor of Preventive Medicine, School of Medicine, Western Reserve University, Cleveland, Maxwell Finland, Associate Professor of Medicine, Boston City Hospital, Boston, Colin M MacLeod, Professor of Research Medicine, School of Medicine, University of Pennsylvania at Philadelphia, K F Meyer, Director Emeritus, George Williams Hooper Foundation, University of California Medical School, San Francisco, John R Paul, Professor of Preventive Medicine, Yale University School of Medicine, New Haven, Conn, Carl F Schmidt, Professor of Pharmacology, School of Medicine, University of Pennsylvania, Philadelphia, and Wesley Spink, Professor of Medicine, University of Minnesota Medical School, Minneapolis

This unit, directed by Charles H Kendall, general counsel of the office of civil and defense mobilization, will examine any charges that have been made reflecting on the integrity of employee actions related to decisions in specific cases The committee will also look into charges that there has been too close a relationship between some employees of the Food and Drug Administration and companies which they are charged by law with regulating

DEATHS

Hale, Arthur Stanley Ⓜ Detroit, University of Toronto Faculty of Medicine, Toronto, Ont , Canada, 1922, specialist certified by the American Board of Ophthalmology, member of the American Academy of Ophthalmology and Otolaryngology, past-president of the Detroit Ophthalmology Society, on the staff of the William Beaumont Hospital in Royal Oak, Mich , and the Harper Hospital, where he died May 9, aged 60, of multiple myeloma

Holley, Sion Woodson, Farmingdale, N Y , University of Chicago, the School of Medicine, 1935, interned at the Henry Ford Hospital in Detroit, served a residency at the Sanatorium of the Jewish Consumptives' Relief Society in Spivak, Colo , veteran of World War II, affiliated with the Nassau County Tuberculosis Sanatorium, where he served a residency, died in the Nassau Hospital in Mineola May 13, aged 53, of ventral hernia

Hunt, Alexander P , Portsmouth, Ohio, University of Louisville (Ky) Medical Department, 1911, member of the American Academy of General Practice, a surgeon for the Chesapeake and Ohio Railway and Norfolk & Western Railway Company, affiliated with the Portsmouth General Hospital and the Smith-Everett Hospital, where he died May 10, aged 75, of myocardial infarction

Irby, William Walter, Meridian, Miss , Mississippi Medical College, Meridian, 1910, died in the Anderson Infirmary May 12, aged 79, of acute coronary thrombosis

Jones, Ernest William, Rusk, Texas, Baylor University College of Medicine, Dallas, 1928, veteran of World War II, on the staff of the Rusk State Hospital, died May 10, aged 57, of pulmonary embolus due to carcinoma of the lung

Josephy, Herman, Chicago, born in Schwaan, Germany, March 27, 1887, Universitat Rostock Medizinische Fakultat, Rostock, Mecklenburg, Germany, 1910 specialist certified by the American Board of Psychiatry and Neurology, Inc , and the American Board of Pathology, fellow of the American Academy of Neurology, member of the American Association of Pathologists and Bacteriologists, vice-president of the American Academy for Cerebral Palsy, formerly on the faculty of the Chicago Medical School, served on the staffs of the Bethany Methodist, Swedish Covenant, and the Chicago State hospitals, died in the Presbyterian-St Luke s Hospital May 19, aged 73, of cerebral thrombosis

Krellenstein, Irving Bernard, Glendale, Calif , Cornell University Medical College, New York City, 1910, fellow of the American College of Surgeons, died in the Behrens Memorial Hospital March 23, aged 68, of arteriosclerotic coronary artery disease

Lee, Reuben N , Chattanooga, Tenn , Medical Department of Grant University, Chattanooga, 1907, died May 5, aged 76, of coronary occlusion

LeFevre, Edgar Brown, Inwood, W Va , University of Maryland School of Medicine, Baltimore, 1905, died in the City Hospital Martinsburg May 14, aged 79, of multiple burns and shock

Linder, Maurice Milton Ⓜ Dayton, Ohio, Ohio State University College of Medicine, Columbus, 1922, member of the American Academy of General Practice, associated with Miami Valley, Good Samaritan, and St Elizabeth hospitals, died May 8, aged 63, of a heart attack

Lohmann, Hermann Gerhard Heinrich, Oakland, Calif , Philipps-Universitat Medizinische Fakultat, Marburg, Prussia, Germany, 1921, died March 13, aged 68, of a heart attack

McCowan, James Augustus, Marietta, Ohio, Starling Medical College, Columbus, 1902, veteran of World War I, for many years county coroner, died May 9, aged 84, of arteriosclerotic heart disease

Mayerberg, Emil R Ⓜ Wilmington, Del , born in 1892, Jefferson Medical College of Philadelphia, 1916, specialist certified by the American Board of Otolaryngology, member of the American Academy of Ophthalmology and Otolaryngology, fellow of the American College of Surgeons, past-president of the Medical Society of Delaware and the New Castle County Medical Society, past-president of the city board of health, for many years member of the Delaware Commission for the Blind, at the beginning of World War I, held a commission as first lieutenant and was placed on the advisory board in Delaware, during World War II also served on the advisory medical board and later the Delaware Appeal Board, on which he served more than two years, received the Congressional Medal of Merit and citation, on the staffs of the Delaware Hospital and the Wilmington General Hospital, died in the Memorial Hospital May 8, aged 68, of coronary arteriosclerosis

Meek, Florence Adrienne, Lewiston, N Y , Ohio State University College of Medicine, Columbus, 1923, formerly practiced in Cleveland, where she

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Ⓜ Indicates Member of the American Medical Association

was associated with the Huron Road Hospital, died May 7, aged 76, of burns incurred in a fire as the result of smoking

Merritt, Charles Walter, St Joseph, Mich, College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905, served as president of the Berrien County Medical Society veteran of World War I, for two terms president of the board of education, for many years a medical examiner for the Metropolitan Life Insurance Company, associated with Mercy Hospital, Benton Harbor, and Memorial Hospital, died May 2, aged 79, of coronary occlusion

Newton, Zachariah Boardman Ⓜ Philadelphia, University of Pennsylvania School of Medicine, Philadelphia, 1927, associated with the Germantown Dispensary and Hospital and the Chestnut Hill Hospital, specialist certified by the American Board of Obstetrics and Gynecology, died at Lake Pytonga, Gracefield, Que, Canada, May 18, aged 59, of coronary thrombosis

Pennington, Love Elree, Jackson, Miss, born in Decatur, Feb 1, 1890, Atlanta Medical College 1915, veteran of World War I, specialist certified by the American Board of Psychiatry and Neurology, member of the American Psychiatric Association, past-president of the Baldwin County (Ga) Medical Society, from 1920 to 1928 chief of staff at the Logansport (Ind) State Hospital, from 1928 to 1944 owner of the Pennington Sanitarium in South Bend, Ind, served as superintendent of the Madison State Hospital in North Madison and the Milledgeville (Ga) State Hospital, served as clinical director of the Terrell State Hospital in Terrell, Texas, and on the staff of the Mississippi State Hospital in Whitfield, on the staff of the Veterans Administration Hospital, clinical instructor at the University of Mississippi Medical Center, attending physician to the University Hospital, died in St Dominic-Jackson Memorial Hospital May 17, aged 70, of coronary thrombosis

Prevo, Samuel Bradley Ⓜ Nashville, Tenn, born in Lawrenceville, Ill, Aug 31, 1909, George Washington University School of Medicine, Washington, D C, 1937, specialist certified by the American Board of Orthopaedic Surgery, member of the Clinical Orthopaedic Society, Southeastern Surgical Congress, and the American Academy of Orthopaedic Surgeons, fellow of the American College of Surgeons, served on the faculty of his alma mater, assistant professor of clinical orthopedic surgery at Vanderbilt University School of Medicine, veteran of World War II and received the Soldier Medal, Bronze Star, and Air Medal, associated with the Vanderbilt University Hospital Nashville General Hospital, Baptist Hospital, St Thomas Hospital, and the Junior League Home for Crippled Children, died May 11, aged 50

Quinn, John Joseph, Athol, Mass, Baltimore Medical College, 1903, formerly practiced in Chicago and East Douglas, Mass, died May 20, aged 82, of a heart attack

Ramsay, James Graham Ⓜ Washington, N C, University of Pennsylvania School of Medicine, Philadelphia, 1922, member of the Southeastern Surgical Congress, fellow of the American College of Surgeons, veteran of World War I, served on the staffs of the Rowan Memorial Hospital in Salisbury and the Tayloe Hospital in Washington, died in Southern Pines May 7, aged 63, of a heart attack

Rawiszer, Hubert, Atlanta, Ga, Atlanta Medical College, 1914, member of the American Academy of General Practice, died May 2, aged 75, of arteriosclerotic heart disease

Reed, Harry Grant Ⓜ Binghamton, N Y, Syracuse University College of Medicine, 1932, fellow of the American College of Surgeons, veteran of World War II, served on the staffs of the Charles S Wilson Memorial Hospital in Johnson City, Binghamton City Hospital, and Our Lady of Lourdes Hospital, died May 6, aged 49, of coronary sclerosis

Richardson, Archie M, Tarentum, Pa, Hahnemann Medical College and Hospital of Philadelphia, 1924, member of the American Academy of General Practice, veteran of World War I, school doctor of the Tarentum school district, on the staff of the Allegheny Valley Hospital, died May 14, aged 64, of lobar pneumonia

Richardson, Mary Lucas, Seattle, University of Colorado School of Medicine, Denver, 1938, specialist certified by the American Board of Pediatrics, interned at the Bryan Memorial Hospital in Lincoln, Neb, where she served a residency, served a residency at St Christopher's Hospital for Children in Philadelphia, member of the American Academy of Pediatrics, formerly chief of the rheumatic heart division of the Pennsylvania Department of Health, died in the Maynard Hospital May 5, aged 75, of cerebral hemorrhage

Ritsema, John Ⓜ Sebewaing, Mich, University of Michigan Medical School, Ann Arbor, 1925, member of the American Academy of General Practice, served as president of the Huron County Medical Society, president of the board of education, associated with the Mercy and General hospitals in Bay City, died May 18, aged 59, of coronary thrombosis

Robinson, Elliott Stirling Andrew Ⓜ Haverhill, N H, Yale University School of Medicine, New Haven, Conn, 1918, formerly on the faculty of his alma mater, Harvard Medical School, and the Harvard School of Public Health, fellow, National Research Council, 1922-1923, served as director of the division of biologic laboratories, Massachusetts

Department of Public Health, veteran of World Wars I and II, died May 5, aged 65, of carcinoma of the gallbladder

Rocho, Victor Luman, Portland, Ore , Hahnemann Medical College of the Pacific, San Francisco, 1913, veteran of World War I, died May 16, aged 72, of cancer of the stomach

Rollins, Herbert Bailey, Florence, Ala , Baylor University College of Medicine, Dallas, 1930, veteran of World War II, medical officer with Tennessee Valley Authority, died May 23, aged 55, of myocardial infarction

Rosenthal, Raoul Simon, Dallas, Texas, Baylor University College of Medicine, Dallas, 1934, fellow of the International College of Surgeons, veteran of World War II, interned at the Parkland Hospital, on the staffs of the Baylor University and St Paul's hospitals, died May 25, aged 50, of acute myocardial infarction

St Lawrence, William, Southampton, N Y , Cornell University Medical College, New York City, 1910, specialist certified by the American Board of Pediatrics, member of the American Academy of Pediatrics, veteran of World War I, served on the staffs of the Central Suffolk Hospital in Riverhead, Stamford (Conn) Hospital, and the Southampton Hospital, where he died June 3, aged 72

Schmorr, Arthur, Port Chester, N Y , New York Homeopathic Medical College and Flower Hospital, New York City, 1926, died May 17, aged 59, of heart failure

Shanklin, Richard Vair Ⓜ Bluefield, W Va , Medical College of Ohio, Cincinnati, 1900, past-president of the McDowell County Medical Society, served as chief physician for the United States Coal and Coke Company and succeeding companies at Gary from 1902 until his retirement in 1946, died May 20, aged 86, of coronary thrombosis

Shappell, Albert Joseph Ⓜ Yonkers, N Y , University and Bellevue Hospital Medical College, New York City, 1934, member of the American Academy of General Practice, on the staffs of the Yonkers General, St Joseph's, and Yonkers Professional hospitals, died May 11, aged 59, of acute coronary infarction

Shields, Daniel Francis, New York City, Washington University School of Medicine, St Louis, 1905, associated with the Bronx Eye and Ear Infirmary, died in St Barnabas Hospital for Chronic Diseases April 28, aged 84, of arteriosclerotic cardiovascular disease

Shiring, Francis Joseph Ⓜ Pittsburgh, St Louis University School of Medicine, 1934, fellow of the American College of Surgeons, specialist certified by the American Board of Surgery, served on the faculty of the University of Pittsburgh School of Medicine, veteran of World War II, city police and fire surgeon, on the staffs of the Pittsburgh and Presbyterian hospitals, died May 18, aged 50, of coronary thrombosis

Simmons, Edward Lincoln, Palo Alto, Calif , University of Southern California School of Medicine, Los Angeles, 1949, member of the American Psychiatric Association, served on the staff of the Palo Alto–Stanford Hospital, died May 27, aged 45, of cardiac failure

Stivers, Moses Ashby Ⓜ Middletown, N Y , Columbia University College of Physicians and Surgeons New York City, 1894, fellow of the American College of Surgeons, veteran of World War I, consulting surgeon at the E A Horton Memorial Hospital, where he died June 3, aged 87, of uremia and diabetes

Streeter, Howard Alvertus Ⓜ Manchester, N H , Boston University School of Medicine, 1898, served as health officer, died May 16, aged 84, of cerebral thrombosis

Trufant, Lester Hall Ⓜ Oberlin, Ohio, McGill University Faculty of Medicine, Montreal, Que , Canada, 1907, member of the American Academy of General Practice, served as president of the Lorain County Medical Society, of which he was secretary-treasurer, associated with the Allen Hospital, where he was president of the medical staff, died in the Cleveland Clinic Hospital June 3, aged 77, of ruptured aortic aneurysm

Van Cor, Chester Arthur, Middletown, Conn , University of Vermont College of Medicine, Burlington, 1914, senior physician at the Connecticut State Hospital for many years, died June 7, aged 75, of cerebral thrombosis

Wayne, Walter W, Long Island City, N Y, Uniwersytet Jozefa Pilsudskiego Warszawa, Poland, 1934, died in the University Hospital, New York City, May 21, aged 52, of myocardial infarction

Wilson, Owen Harris Ⓜ Nashville, Tenn , born in Sandersville, July 20, 1870, Vanderbilt University School of Medicine, Nashville, 1891, for many years on the faculty of his alma mater, on June 3, 1948, was honor guest at a dinner attended by more than 200 medical men of Nashville and Middle Tennessee, given by the Nashville Pediatric Society, and was presented with a bronze plaque commemorating his long service in the field of medicine, together with a testimonial volume, and a commission as an honorary colonel on the staff of Gov Jim McCord, past-president of the Tennessee Pediatric Society, author of "Care and Feeding of Southern Babies A Guide for Mothers, Nurses and Baby Welfare Workers of the South," died May 10 aged 89 of myocardial infarction

FOREIGN LETTERS

INDIA

Bronchopleural Fistula—S S Anand and co-workers (*Indian J Chest Dis* 2 19 [Jan] 1960) reported that in a series of 138 patients who had lung resections, bronchopleural fistula developed in 20 (14 5%) Of all the procedures used, the greatest number of fistulas occurred after pneumonectomy and the next greatest after lobectomy With conservative treatment of this complication, the authors obtained successful results in 13 of 20 patients To prevent bronchopleural fistula, they stress a longer preoperative management of patients and certain points in operative technique such as high division of the bronchial stump, with care taken not to devascularize it, and coverage of the stump with living intrathoracic tissue In the postoperative management, rapid elimination of the dead space is important, for this they recommend adequate physiotherapy and tube drainage If the remaining lung fails to fill the pleural cavity, early thoracoplasty should be resorted to

Superficial Infections in the Neonate—J N Pohowalla and co-workers (*Indian J Child Hlth* 9 231 [May] 1960) investigated the nature and incidence of superficial infections in neonates in a general hospital Of the 1,298 live births, 236 neonates (18 2%) showed evidence of such superficial infections as conjunctivitis, stomatitis, and dermatitis Cultures revealed 66 strains of organisms including staphylococci, Escherichia coli, Pseudomonas aeruginosa, streptococci, and Candida tropicalis Many pathogens in this series were resistant to antibiotics Although there were 13 deaths in the series, all but 2 occurred in premature infants The authors concluded that superficial infection by itself was not responsible for the deaths They believed that the high incidence of these infections might be related to such factors as obstetric complications, overcrowding in maternity wards, and free access of visitors to these wards

Streptomycin Resistance of Mycobacterium Tuberculosis—Chandrashekhar and Venkitasubramanian (*Indian J Chest Dis* 2 48 [Jan] 1960) stated that many workers have reported alterations in the ribonucleic acid content of streptomycin-resistant strains of such organisms as Staphylococcus aureus, Escherichia coli, and Salmonella enteritidis The authors tried to determine whether any such alterations occur also in the case of Mycobacterium tuberculosis A strain of tubercle bacilli was made resistant to 1, 10, and 100 mcg , of streptomycin, and the nucleic acid content was determined The results showed an increase in the resistant as compared to the sensitive strain, but the content of deoxyribonucleic acid showed a slight decrease Estimations of total phosphorus and total lipid levels made simultaneously showed no change in the total phosphorus level in the resistant strains, but the total lipid levels were increased in the resistant strains

New Tetracycline—Agarwal and Chatru reported encouraging results with pyrrolidinomethyl tetracycline They used it to treat 14 patients who had such infections as acute appendicitis with abscess or perforation, diabetes with carbuncle, cholecystitis, acute salpingo-oophoritis, acute pancreatitis, and intestinal perforation The drug was given intravenously in an average dose of 250 mg twice a day Tetracycline was given by mouth as soon as the fever and toxemia were controlled

In all these patients the pyrrolidinomethyl tetracycline was used postoperatively The temperature usually came down by lysis, reaching normal in three or four days Concomitant improvement in the general condition was also observed A patient who had tuberculosis of the spine with pyemic abscess who had failed to respond to streptomycin alone showed a remarkable improvement when the new drug was given in addition No untoward reactions were noticed Two of the 14 patients died, one with mesenteric thrombosis and the other with acute hemorrhagic pancreatitis Since the drug can be given intravenously, its effect is rapid It can also be given to elderly patients who have myocardial damage or renal disorders in whom the amount of fluids to be administered intravenously is restricted It can also be useful in domiciliary practice when the drip method may not be suitable

New Sulfonamide—I M DeSa Souza (*Current M Pract* 4 189 [April] 1960) treated 79 patients who had pyelitis with a new sulfonamide, sulfophenyl pyrazol He gave two tablets twice a day for three days followed by one tablet twice a day for three days The infective organisms in acute cases were staphylococci and hemolytic streptococci, alone or together, and in chronic cases Escherichia coli and Pseudomonas aeruginosa were also seen The results showed that this new compound was successful in the treatment of patients with pyelitis caused by staphylococci or hemolytic streptococci These patients responded to a single course of six days of oral therapy In severe cases, it controlled the

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The items in these letters are contributed by regular correspondents in the various foreign countries

clinical symptoms within three to six days A single course, however, was not sufficient to cause reduction in the number of colonies of streptococcus and staphylococcus or the number of pus cells and the amount of albumin in urine, for which a second or even a third course of six days each, at intervals of six days, was necessary The drug had no effect on infections by E coli or P aeruginosa In these patients it neither produced clinical relief nor had any effect on the number of colonies grown from urine culture

SWEDEN

Digital Arthrodesis—Selective arthrodesis is helpful in restoring hand function in many circumstances When grip and digital function are impaired because of joint destruction, irreparable damage to joint-stabilizing ligaments, or flail joints resulting from irreversible motor loss, solid arthrodesis in a functional position is desirable In peripheral nerve palsies, selective arthrodesis of digital joints may augment function Moberg and Henrikson (*Acta chir scandinav* 118 331-338, 1959-1960) studied a series of 150 patients with arthrodeses of hand joints There were 85 patients with arthrodesis of proximal interphalangeal joints of whom 71 were followed up, 27 with arthrodesis of the metacarpophalangeal joint of the thumb of whom 21 were followed up, 32 with arthrodesis of distal joints of all digits of whom 21 were followed up, and 6 with arthrodesis of carpometacarpal joints of the thumb, all of whom were followed up Of these 150 arthrodeses, all but two healed without infection The most rapid and reliable healing in proximal interphalangeal joints was obtained by using a stabilizing bone peg Other methods of internal fixation, such as Kirschner wires with or without small bone grafts, gave poorer results The most rapid healing in metacarpophalangeal joints resulted when bone graft fixation was used The results after fusion of the distal interphalangeal joints did not vary significantly with the various techniques used The marked improvement in function after fusion of appropriate joints bore out the advisability of its use in most of these patients When normal painless joint function cannot be restored, arthrodesis should be considered

The Dumping Syndrome—Sten Wallensten (*Acta chir scandinav* 118 278-285, 1959-1960) reported the results of conversion of a Billroth 2 to a Billroth 1 gastrectomy in 18 patients suffering from severe dumping symptoms The Billroth 1 operation was supplemented with vagotomy in one patient This measure was effective in relieving the dumping symptoms, but the tendency to recurrence was increased The author recommended that the Billroth 1 operation be supplemented with vagotomy Roentgenocinematography of small intestinal motility and determination of plasma volume after dumping provocation with 50% glucose solution given orally were of great aid when assessing the indications for reoperating on these patients These tests also afforded objective evidence on the effectiveness and results of the surgical measure The author recommended their wide use

Caliber of the Pancreatic Ducts—More exact knowledge of the caliber and relations of the pancreatic ducts under normal and abnormal conditions would be of clinical value Erik Millbourn (*Acta chir scandinav* 118 286-303, 1959-1960) examined 200 corpses with cholangiography after tying off the papilla of Vater, supplemented, when necessary, with pancreaticography via the caudal region of the pancreatic duct The author analyzed several aspects of 167 suitable cases in which no biliary or pancreatic disorder was present In 150 cases in which the pancreatic duct served as the main or sole outlet for the pancreatic secretion, it was observed that caliber was not related to sex Between the ages of 20 and 30 years the mean maximal diameter of the pancreatic duct was 3 3 to 3 5 mm It increased successively with age and reached a diameter of 4 2 mm at 50 years, and ranged between 5 and 6 mm after 70

The widest part of the pancreatic duct was almost invariably situated in the head of the pancreas, 1 to 3 cm from the duct's opening in the common bile duct With few exceptions its caliber decreased peripherally to almost zero at the tip of the tail of the pancreas Individual variations were marked Fine-caliber ducts 2 5 to 3 0 mm in diameter occurred in all age groups up to 80 years On the other hand, large-caliber ducts of 5 mm or more were noted only above the age of 31 years The maximal calibers of the pancreatic and common bile ducts show some correspondence, suggesting that the sphincter of Oddi generally acts as a functional entity, but under normal, pathophysiological, and pathological conditions the pancreatic and choledochal sphincters may act as different functional units, differing markedly in muscular strength A constriction which measured on the average of 0 2 mm in length and with a mean diameter of 1 8 mm was commonly present in the segment of the pancreatic duct adjacent to its orifice The present study afforded no indication as to its cause Ampulla-like dilatation of the terminal portion of the pancreatic duct was rare In the presence of an accessory duct capable of subsituting for the pancreatic duct, the latter was of smaller caliber than otherwise

If the values recorded in this autopsy study were to be used as a measure of the normality or otherwise of the caliber of the pancreatic duct on cholangiography or pancreaticography at operation or after operation, they should be reduced throughout by about 1 mm in the various age groups In 17 cases in which the accessory duct served as the main or sole outlet for the pancreatic secretion, the largest caliber of the accessory duct with this function was about 1 mm less than that of the pancreatic duct This might be attributable in part to the fact that the accessory duct had no mechanism resembling the sphincter of Oddi in its duodenal orifice This agrees with the author's observation of the fairly frequent presence in the orifice of the accessory duct of an ampulla-like dilatation, irrespective of whether the duct served as the sole or the main outlet or in its accessory capacity The relatively small, isolated Wirsung system present when the accessory duct served as the main outlet of the pancreas was of striking caliber having a mean diameter of 2 4 mm

Postcommissurotomy Syndrome.—The postcommissurotomy syndrome consists of pains retrosternally and in the left half of the thorax in combination with a moderate rise in temperature, which occurs suddenly one or more weeks after valvulotomy The symptoms persist for 10 days to 4 weeks Bagger-Dahlstrom and Malmstrom (*Acta chir scandinav* [supp] 245 193-196, 1959) observed symptoms resembling postcommissurotomy syndrome among 106 patients operated on for mitral stenosis The postoperative observation period averaged 64 days Postcommissurotomy syndrome appeared in 10 of these 106 patients The syndrome was characterized by a temporary secondary exacerbation of the postoperative symptoms, an elevated sedimentation rate, pleural and pericardial exudate, or both, and pains in the region of the left shoulder The syndrome appeared in 2 of 33 patients who were undergoing postoperative treatment with cortisone In a number of patients the condition caused great subjective discomfort The prognosis was good

UNITED KINGDOM

When Foods are Drugs—The Ministry of Health is distributing a handbook to all general practitioners in the health service to enable them to determine whether a substance is a drug or a food Doctors are unable to prescribe foods for National Health Service patients In the past, several doctors have prescribed brandy and glucose for sick patients, only to find that they have had to pay for these themselves The new handbook was produced by a committee of doctors and pharmacists and will enable a doctor to decide whether a substance he is prescribing is a drug or a food

Decisions on the classification of borderline substances as foods or drugs must to some extent be arbitrary, but the committee has set up the following principles for the guidance of physicians 1 Substances which are primarily nutritional and can be used by healthy people should be classed as foods 2 Foods manufactured especially for the treatment of disease shoud be classified as drugs 3 Compounds in which the main constituents are foods should be classed as foods, even when they are used as drugs 4 Alcoholic beverages such as brandy are not to be regarded as drugs

The use to which a preparation is put and the manner in which it is given may determine the classification Thus glucose given intravenously or in compressed tablets to diabetics is a drug, but given as a powder with or after meals it is a food Barley sugar, milk foods, foods for invalids, vitaminized foods, all forms of drinkable alcohol, meat extracts, saccharin, iodized salt, and mineral waters are classified as foods, but special milk preparations used, for example, in the treatment of infantile allergy, eczema, and sprue are classed as drugs, as are concentrated milk foods such as casein and protein hydrolysates The classification of vitamins depends on how they are used If prescribed to remedy a vitamin deficiency they are drugs, otherwise they are foods and not prescribable

Doctors are also advised not to prescribe preparations of undisclosed composition or preparations used for cosmetic purposes The latter include sun and insect repellant creams, medicated soaps, even if used by patients with allergic or trophic skin reactions, and disinfectants likely to be used for domestic purposes The committee emphasized that its recommendations are advisory only and not mandatory There is provision for an appeal to an independent referee A physician runs the risk of having to pay for his patient's prescription if it falls into the category of a food or cosmetic preparation

Vacuum Extractor in Obstetrics—A modification of the apparatus of Malmstrom for the extraction of the fetus by the application of a suction cup to the head was described by Chalmers and Fothergill (*Brit M J* 1 1684, 1960) This procedure was devised as an alternative to the use of forceps The instrument has three metal cups, 20 mm deep and 40, 50, and 60 mm in diameter, respectively, the size used depending on that of the presenting part From a plate within the apex of each cup a chain passes inside a flexible rubber tube to a traction bar, and from this a further rubber tube passes to a vacuum bottle, which can be evacuated by means of a pump

With a cephalic presentation the largest possible cup is applied well back on the head to promote flexion, after the membranes have been ruptured A pressure of 0 6 to 0 8 kg per square centimeter is gradually exerted on the head over a period of 6 to 10 minutes, to fill the cup with loose scalp Traction is then applied in the axis of the pelvis by pulling on the traction bar, traction coinciding with the pains When the infant is delivered the scalp is released by opening a screw valve in the cup Frequently no anesthesia is required, but local perineal infiltration or pudendal block can be used

The method is less painful and dangerous than the use of forceps, and it involves less danger of sepsis No instrument occupies the birth canal, all the available space of which is free for the passage of the fetus Excessive traction causes the suction cup to be detached and does not damage the fetal head The cup raises a large caput, but this subsides in a few hours One of the advantages of this method over the use of forceps is that it can be applied in the delayed first stage of labor to promote dilatation of the cervix in a physiologic manner It replaces forceps in a wide range of conditions, although it is unsuitable where acute fetal distress or a severe degree of cephalopelvic disproportion exists

Adrenalectomy and Hypophysectomy for Breast Cancer.—Three years ago Atkins and co-workers reported a series of 30 patients with advanced cancer of the breast operated on by bilateral adrenalectomy with oophorectomy and 30 operated on by hypophysectomy At that time a comparison of the two series favored hypophysectomy, but the results were not conclusive Since then the numbers have been more than doubled, making possible a more effective comparison between the two groups A further report was made on 79 patients operated on by adrenalectomy with oophorectomy and 70 operated on by hypophysectomy (*Lancet* 1 1148, 1960) All patients had previously undergone a radical mastectomy, or their disease was so widespread that treatment by surgery, irradiation, and hormones could no longer be considered

All patients were offered operation, since they had nothing to lose and the choice of type of operation was by random selection All lesions were accurately measured and photographed if visible, and roentgenograms of bone metastases were taken before and after the operation Skull roentgenograms were obtained of patients selected for hypophysectomy Estimations were made of hemoglobin level, white blood cell and differential counts, sedimentation rate, serum cholesterol and alkaline phosphatase levels, and the urinary excretion of estrogens, pregnandiol, 17-oxosteroids, 17-oxogenic steroids, androsterone, dehydroepiandrosterone, etiocholanolone, pooled 11-oxy-17-oxosteroids, and gonadotropins Cortisone was given to all patients postoperatively The postoperative condition was assessed every month by examining each lesion, grading it numerically, adding up the numbers, averaging them, and multiplying the figure obtained by six to bring it to a less unwieldy number This figure was called the average clinical value (ACV)

Analysis of the results showed that hypophysectomy had a more favorable effect on the patient with advanced breast cancer than did bilateral adrenalectomy with oophorectomy The difference was revealed both by an analysis of survival rates, which were 20 3 and 14 2 months, respectively in the two groups and by the ACV, which over the survival period averaged 6 57 and 5 48, respectively, in the hypophysectomized and adrenalectomized groups At all periods the ACV of the former group of patients was greater than that of the other The difference between the ACV of the two operations was well within the 5% level of probability

The response of metastatic breast cancer to adrenalectomy or hypophysectomy largely depends on the hormonal environment in which the tumor is growing Bulbrook and co-workers (*Lancet* 1 1154, 1960) working in cooperation with Atkins and his group, showed that, of the hormonal factors measured, the levels of etiocholanolone and the 17-hydroxycorticosteroids are the most useful in predicting the outcome of the two operations, particularly in indicating the probable response to hypophysectomy The mean 17-hydroxycorticosteroid level proved to be higher and the mean etiocholanolone level lower in those patients in whom hypophysectomy and adrenalectomy were a failure than in those in whom the operations produced remission The ratio between the two values gave an even better prediction of the outcome of the operation

Rheumatoid Neuropathy.—Over the past few years it has become apparent that rheumatoid arthritis is a generalized disease with systemic as well as joint manifestations Hart and Golding (*Brit M J* 1 1594, 1960) and Steinberg (*Ibid* 1 1600, 1960) described the occurrence of peripheral neuropathy as part of the symptoms of patients with rheumatoid arthritis Hart and Golding have observed it in 42 patients (18 men and 24 women) This relatively high incidence in men is in line with that in other types of peripheral neuritis Steinberg found that this form of neuropathy was associated with steroid therapy in over 80% of his patients, but in those seen by Hart and Golding it occurred in 12 who had never been given corticosteroids They considered it a part or a complication of rheumatoid arthritis and termed it rheumatoid neuropathy Certainly patients with the worst cases and all with fatal ones had received corticosteroids, and sudden withdrawal or changing of the type of corticosteroid seemed to precipitate this complication

The neuropathy is usually symmetrical and is primarily sensory, motor manifestations occurring in the more severe cases Feet and legs are more often affected than hands and arms According to Hart and Golding, rheumatoid neuropathy occurs more frequently in patients with nodules and with advanced rheumatoid disease, usually with a high-titer positive differential agglutination test (Rose-Waaler test), marked changes in the electrophoretic pattern, and polyarteritic and neuropathic features Arteritis and vascular necrotic finger lesions may coexist The finding of a diffuse arteriopathy at autopsy suggested that the probable cause was an arteritis of the vasa vasorum Arteritis of the peripheral nerves was seen in some of Steinberg's patients Although mild cases do occur and many patients recover spontaneously, rheumatoid neuropathy should in general be regarded as a serious complication and one associated with a poor prognosis Several patients in the two groups studied died within a year of onset of the neuropathy No form of therapy has been found to be effective

Antibodies After Poliomyelitis Vaccination—Kendall and co-workers (*Brit M J* 1 1689, 1960) determined the level of antibody response after periods of up to two years after a course of two injections of poliomyelitis vaccine, followed by a third (booster) dose six months later The subjects were schoolboys and adolescents The results showed that neutralizing antibodies to types 2 and 3 poliovirus persisted at a much higher level than antibody to type 1 when tests were made 18 to 24 months after a third dose of vaccine The persistence of antibody after this was shown to depend on whether antibody induced by the two primary doses of vaccine was present at the time the third dose was given

After the third dose, the average fall in titer for all types was from 76 to 81% in 18 to 24 months After vaccination with type 1 virus, neutralizing antibody fell by 75% after a year to 88% of its peak value after two years, but decline in antibody was found to vary widely from person to person The authors believe that, until a more potent type 1 vaccine component is available, a fourth dose of the vaccine should be given two years after the third

Similar results were obtained in children by Logan and co-workers (*Brit M J* 1 1692, 1960), who reported a decrease of nearly 80% in antibody titer for all three virus types two years after the first dose of poliomyelitis vaccine A good response to a fourth dose given two years after the first was found in nearly all the children

Oral Mucosal Cells in Pernicious Anemia—Farrant (*Brit M J* 1 1694, 1960) examined cytologically oral squamous mucosal cells of patients with pernicious anemia before and after treatment Films of oral mucosa were obtained by scraping the inside of the cheek with a microscope slide and then drying and staining the material by the May-Grunwald-Giemsa technique An image of the buccal squamous cells and their nuclei was projected from the microscope to a ground glass screen to give a magnification of 1,000 Measurements were made of the long and short axes of the nuclei of these cells from patients with pernicious anemia before and after treatment and at intervals up to 32 months after the blood had shown maximal improvement

Criteria of diagnosis were typical macrocytic blood film, megaloblastic bone marrow, histamine fast achlorhydria, and satisfactory response to vitamin B_{12} or liver extract All patients showed a highly significant decrease in nuclear size of the oral mucosal cells after treatment, the decrease being greater in the short axis Not only did the nuclei become smaller and more uniform in shape, but in many cases the nuclear chromatin became more pyknotic and dense Before treatment, most of the nuclei were irregular and asymmetrical in outline After treatment they became more regular in appearance, like the nuclei from the buccal mucosa of normal subjects The change of nuclei to normal shape and size occurred in only a few days once treatment was started In comparison the time needed for a smooth tongue to become normal was much longer

Response of Diabetes to Sodium Orthocresotinate—Acetylsalicylic acid (Aspirin) in large doses relieves mild diabetic symptoms, lowers fasting blood sugar levels, and reduces glycosuria and ketonuria in patients with mild diabetes The dose of acetylsalicylic acid required invariably produces side-effects Sodium orthocresotinate is as effective as acetylsalicylic acid in the treatment of rheumatic fever and even in large doses does not cause side-effects

Lightbody and Reid (*Brit M J* 1 1704, 1960) therefore investigated its action in diabetics It was given in doses of 1 0 to 1 3 Gm five times daily to hospitalized diabetics After dietary restriction, the carbohydrate intake of the patients was kept constant at 120 to 150 Gm daily until the fasting blood sugar level was stable The total caloric intake ranged from 1,300 to 1,700 calories daily At the end of the control period, a course of orthocresotinate was given for at least two weeks Those patients who initially needed insulin were given the drug while the insulin was slowly withdrawn Three diabetics, however, continued to need insulin

Those previously treated by diet alone responded to treatment with orthocresotinate, which relieved mild symptoms of diabetes and caused a fall in fasting blood sugar level and a reduction in glycosuria in all patients Those requiring insulin needed much less while taking the drug One patient was able to achieve satisfactory control of the disease by replacing insulin completely with orthocresotinate No deafness or tinnitus, the complications of treatment with acetylsalicylic acid, were experienced by any of the patients, although temporary headache, anorexia, nausea, and vomiting occurred in some These effects disappeared when the dosage was reduced It was found that a serum level of 30 to 40 mg per 100 ml of orthocresotinate gave a hypoglycemic response comparable to that produced by large doses of acetylsalicylic acid

CORRESPONDENCE

TREATMENT OF CEREBRAL VASCULAR ACCIDENTS

To the Editor —The review of therapy for cerebral vascular accidents by Dr George A Wolf Jr in THE JOURNAL (172 562 [Feb 6] 1960) is a fair statement of the indications, contraindications, and limiting factors of currently accepted regimens I take issue, however, with the statement that treatment during the acute phase of a cerebral vascular accident is limited to the supportive measures listed in this article I should like to call attention to another valuable approach to the management of selected patients with acute and subacute cerebrovascular accidents, particularly those with significant brain stem involvement the use of the adrenocortical steroids My observations in such patients for the past four years (*J Am Geriatrics Soc* 6 686 [Sept] 1958) may be summarized here by stating that dramatic improvement has been observed repeatedly in critically ill patients with clinically progressive cerebral infarction in whom it appeared that remissions either of a spontaneous nature or due to other forms of therapy could be reasonably ruled out Such conclusions seem to be feasible on the basis of the periods of observation prior to institution of hormonal therapy and on the basis of the occurrence of acute relapses noted in several patients when steroids were withdrawn or reduced in dosage, which were then followed by a prompt reversal of this rebound phenomenon with the reinstitution of the previous regimen

The improvement in patients with impaired swallowing, impaired speech, and periodic breathing has been striking While improvement of brain stem function tends to be much more dramatic than that of limb paralysis, it is my impression that the return of motor function in several of these patients was decidedly more rapid than could have been anticipated otherwise This can be attributed to acceleration of the healing process and to facilitation of rehabilitation brought about by minimizing the frequent ravages of complicating reflex sympathetic dystrophy, especially when the shoulder and hand are involved Although these observations apply largely to patients with spontaneous cerebral thrombosis, the same pattern of therapeutic benefit has been noted in several instances of cerebral embolism occurring after myocardial infarction

A striking feature noticed in these long-term studies relates to the improvement of swallowing and speech in patients with subacute and even chronic pseudobulbar palsy It is my conviction that the potential for return of such brain stem function is much greater than has been generally believed possible There is evidence that the benefits described are due largely to the prevention or prompt elimination of interstitial cerebral edema, particularly in the confined area of the brain stem In turn, such treatment permits early restitution of neurological function by minimizing damage to nerve cells until collateral channels have begun to perfuse the ischemic area

Such a dynamic approach to the management of potentially reversible acute and subacute cerebral vascular disease cannot be regarded as indiscriminate adrenocortical steroid therapy In the treatment of the patient with a massive cerebral vascular accident, parenteral steroid therapy has certain advantages over anticoagulant therapy, for at times one cannot be sure that an intracerebral clot is absent, notwithstanding the absence of blood in the spinal fluid Furthermore, there is a decided risk of converting an anemic cerebral infarct into a hemorrhagic one

Some of the discrepancies of results in the literature may be attributable to undue delay in the institution of treatment, inadequate dosage, and unpredictable absorption by the oral route Either 75 to 100 mg of cortisone acetate or 4 mg of dexamethasone every six or eight hours injected into the deltoid area for several days can be used, after which the parenteral dosage is reduced In critical situations, the dexamethasone may be infused intravenously Once improvement is forthcoming, the oral route may be used Except in patients having pseudobulbar palsy, an attempt is made to discontinue steroid therapy by the third week

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REACTION TO BUNAMIODYL

To the Editor —I would like to comment on the article, "Cholecystography with Bunamiodyl," by Meszaros and Rich in THE JOURNAL, April 23, page 1884 I have been using bunamiodyl (Orabilex) in this hospital for the last six months The prescribed dosage has been adhered to, and the examinations are often combined with those of the upper gastrointestinal tract In 111 examinations made with bunamiodye only one patient has had diarrhea, one has had dysuria, and five patients have had a moderate urticaria over the extremities and neck

Bunamiodyl was used as a medium for gallbladder examinations of executives of a large company, and after 43 examinations I had to discontinue its use There were five reactions two patients had a severe esophageal spasm, one patient had a severe urticaria over the extremities and entire trunk, and two patients had a moderately severe urticaria over the extremities These five patients gave no history of allergies None of them were factory workers All of them hold well-paid desk assignments

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ONE POINT OF VIEW

To the Editor —The comments on AMEF and other subjects by Dr Sedgwick Mead, in THE JOURNAL, April 23, page 1972, were read with interest The necessity for maintaining our present physician/population ratio is seriously open to question The acceptance of arbitrary figures, dredged up from whence no-one knows, is unwise For some time I have believed that our present physician/population ratio is unnecessarily high In 14 years of practice I have encountered nowhere a genuine shortage of physicians There is an uneven distribution, but I believe the problem is generally one of too many generals and not enough soldiers, i e, too many who specialize and not enough who do general work Grinding out more and more men who do less and less in order to satisfy theoretical standards is absurd and economically most unwise Actual need is not to be confused with desire to fulfill certain abstract or arbitrary standards

Aldous Huxley, whom Dr Mead quotes, is a great writer Unfortunately, he is not necessarily an authority on medical economics I challenge this well-meaning but somewhat hazy thinker to prove beyond a shadow of a doubt that we are deliberately restricting production of new doctors Perhaps Mr Huxley longs for the premature attainment of his "brave new world," toward which his native Britain has already so far advanced It is indeed part of the duty of a sovereign state to help alleviate any theoretical shortage of physicians This is not a federal responsibility but one for each state to decide Dr Mead should be well aware of the fact that the number of applicants for medical schools, as well as their caliber, has been ominously declining in the last few years In a few years the continuance of this trend might well cause many of our schools to have to beg for applicants, even inferior ones

I am not a member of any conspiratorial medical hierarchy, yet I am opposed to federal aid to medical education as well as to a large number of other federal monetary gifts and aids for a variety of other groups and purposes The reason has nothing to do with racial segregation or integration These things can and should be done by other more efficient and less wasteful ways I am proud of the AMA lobby in Washington May it maintain its stubborn fight against those who are trying to destroy the character of the profession in order to completely control and dominate the American system of living When we finally go under all goes under with us

How many doctors are now recommending to their own sons that they embark on a medical career? After what has happened to medicine since 1932 and what is facing us now, is it any wonder that many physicians can no longer suggest to those they love that they launch themselves into a field whose future is so seriously threatened?

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To the Editor —In THE JOURNAL, April 23, page 1972, appeared a letter from Dr Sedgwick Mead It seems to me that he has stumbled on something when he contends that it is not the responsibility of the doctors to provide the nation with an adequate supply of physicians Neither is it the responsibility of a "sovereign state to see that its people have an adequate supply" The shortage of physicians is due to the lack of inclination on the parts of students and parents to pave the way for themselves by raising an adequate supply of physicians One does not see the clergy forcing people to become clergymen, this has to come from the parents and their offspring

To point out that other fields are becoming more attractive than medicine is merely to beg the question rather than to explain why there *is* shortage of physicians If there is to be a such a shortage it is a sad commentary on the condition of the United States What can a sovereign nation do to stimulate the citizens to supply from their own offspring this adequate supply? This is the nub of the situation and, strangely, one never hears it discussed

I, as a young physician, am tired of hearing the A M A used as a whipping boy—especially when it is done by other physicians Be active in the A M A, support it, and work within the machinery of the A M A laws and by-laws The A. M A lobby has made it possible to have the kind of system that prevails, it has also made it possible for people like Dr Mead and myself to become physicians Our parents have supplied the stimulus for us to become physicians We did not tell the credentials committees of the medical schools our opinion of the A M A If the citizens are indolent and lacking in ideals, do not blame the A M A lobby for the shortage of physicians

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BOOK REVIEWS

Surgery as a Human Experience The Psychodynamics of Surgical Practice By James L Titchener, M D, Assistant Professor of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, and Maurice Levine, M D, Professor of Psychiatry and Director of Department, University of Cincinnati College of Medicine Cloth $6 Pp 285 Oxford University Press, 417 Fifth Ave, New York 16, 1960

With the growing tendency of medical men to specialize, it is no longer possible for any practitioner to be all things to all patients, and the need for an interrelationship of surgical and psychiatric services becomes apparent The authors of this extremely well-written book have delved deeply into the emotional problems of the surgical patient which can affect his recovery and adjustment to his altered condition

Reporting the results of a two-year study of 200 surgical patients selected at random, who were followed up for six months after their operations, the authors have produced a text which is illuminating to the surgeon, the general practitioner, and the patient himself They have investigated preoperative and postoperative depressions, the reaction of patients with psychosomatic illness to operation, the influence of deep-seated emotional stress on recovery, the personality changes that can be expected after the patient has lost a body function or organ, adjustment problems of children and the aged after surgery Danger signals are pointed out, and methods of psychological treatment and guides for referral of the patient to the psychiatrist are presented Reports of surveys by other psychiatric teams are evaluated There is an impressive bibliography and a comprehensive index

The book is aimed at better understanding of the surgical patient, and the authors plead for a closer collaboration between the psychiatrist and the surgeon They urge that some form of psychotherapy be made available during hospitalization for patients who show personality difficulties This is a fascinating text and a pioneering work in its field

PHILIP THOREK, M D

Comprehensive Medical Insurance A Study of Costs, Use, and Attitudes under Two Plans By Odin W Anderson Ph D, Research Director, Health Information Foundation New York and Paul B Sheatsley Health Information Foundation research series 9 Paper Pp 105 Health Information Foundation, 420 Lexington Ave, New York 17 n d

The term "dual choice' as applied to health insurance is relatively new It means that the persons in an employee group may choose one of two alternative insurance plans Sometimes the dual choice can be exercised only once—usually initially, however, in other instances employees are permitted, at intervals, to transfer from one plan to the other Prior to the advent of dual choice systems under contributory group plans most employees had only the alternatives of participation or nonparticipation in a single plan either offered by an employer or negotiated by a union

This publication is listed by Health Information Foundation as Research Series No 9 and described as, 'a study of costs, use, and attitudes under two health insurance plans" The two original objectives of the study were "(1) to analyze to what extent the provision of virtually complete hospital and physicians' services through prepayment helps families to pay for costs of all services in two contrasting methods of organizing physicians' services, and (2) to determine the attitudes toward and perceptions of medical practice that households had who chose Group Health Insurance, Inc (GHI) or Health Insurance Plan of Greater New York (HIP), as well as the reasons for their choice and the impressions they gained of the plan they chose after some experience with it" A third objective emerged which was a comparison of utilization and cost patterns between these two insurance plans which have different methods of paying for the services of physicians GHI pays for professional services on the basis of a benefit schedule whereas HIP uses the so-called group practice approach where physicians are paid on a capitation basis

Persons selected for interviews were members of the Dress Joint Board of the International Ladies Garment Workers Union, International Association of Machinists and Office Employees Union These persons were drawn from a sampling of the subscribers under the two insurance programs To the extent possible, these samples were matched with regard to their socioeconomic status Of the 900 persons selected, interviews were completed with 841 Each person in the survey sample was asked what motivated him to select the plan he chose From among those enrolled in GHI, 72% cited "free choice of physician' Of the HIP enrollees 40% gave nothing to pay' as their reason The next reason most frequently given by each group was others in the shop were joining' The foregoing were listed as spontaneous responses Later the interviewees were shown a listing of reasons following which free choice of doctor" was checked as a reason by 88% of GHI subscribers and "nothing to pay" was a reason checked by 61% of the HIP subscribers

The study report indicates that most enrollees in both plans expressed favorable attitudes toward the plan he selected and toward their physicians Of the GHI subscribers 90% and of the HIP enrollees 79% had favorable attitudes toward their chosen plans Of the HIP subscribers 12% and of the GHI subscribers 3% expressed dissatisfaction with the plan Moreover, more HIP subscribers said, "doctors don t let you explain troubles," and "you wait too long in their offices" when citing dissatisfactions regarding physicians The report showed that very few GHI subscribers changed doctors on joining the plan while 46% of the HIP subscribers did so

The main portion of the text deals with costs of health care services, proportion of costs paid by insurance, utilization of services, background on choice, attitudes, and experiences as well as summary and conclusions The five appendixes discuss methodology, estimates of sampling errors, composition of samples, costs for families, and costs for three union groups The study report indicates that there were more hospital admissions, surgical procedures requiring hospitalization of the patient, and nonhospital surgical procedures per 100 subscribers for GHI than for HIP enrollees Such data seemingly are at variance with pronouncements of certain protagonists for group practice coordinated plans to the effect that other program benefits are deterrents to the timely seeking of health care Enrollees under both groups had about the same number of physicians' home, office, and hospital calls, and about the same proportion of both groups did not see a physician during the period of the survey

The book is well indexed A number of the tables presented relate to previous studies undertaken or sponsored by the Health Information Foundation Some of the tables, however, are not explained sufficiently to have much meaning to those who are uninitiated in statistical studies

Howard O Brower

Principles of Animal Virology By F M Burnet, Director, Walter and Eliza Hall, Institute of Medical Research, Melbourne, Australia Second edition Cloth $12 Pp 490, with 34 illustrations Academic Press, Inc , 111 Fifth Ave , New York 3, Academic Press, Inc (London), Ltd , 17 Old Queen St , London, S W 1, England, 1960

Virology has advanced with unprecedented rapidity in the last decade, making a second edition of this book necessary The author states, "the etiologies are defined, the principles of immunization are well known, the routine of diagnosis, of vaccine production, of public health action, can run smoothly " The term "animal viruses" is used to designate viruses found in the animal kingdom as opposed to "plant viruses " The first chapters on the history and general problems of animal virology are excellent as are the succeeding chapters on cellular infection, pathogenesis, and immunity Other chapters discuss active and passive immunity, latent infections, and the ecological aspects of viral disease The variation and evolution of the viruses are stressed, and the author predicts there will be a new influenza A virus within 20 years whereas another enterovirus will become the major cause of poliomyelitis within 50 years The final chapter is devoted to classification and nomenclature of viruses, presenting the "official" suggestion of four groups of pathogens in humans and the "nonofficial" suggestion of nine groups Another decade of investigation will show great progress in these matters The numerous references at the end of each chapter represent excellent background material on the subject of viruses

Thomas G Hull, Ph D

Genetic Basis of Morphological Variation An Evaluation and Application of the Twin Study Method By Richard H Osborne and Frances V De George Study conducted at Columbia-Presbyterian Medical Center under auspices of Institute for Study of Human Variation, Columbia University Cloth $5 Pp 204, with illustrations Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass , Oxford University Press, Amen House, Warwick Sq , London, E C 4, England, 1959

This monograph presents a brief review of the methodology of twin studies and the results of applying some of these methods to a series of measurements on a group of monozygotic and dizygotic twins In addition to containing variance analyses for detecting genetic components in 62 classical anthropometric measures, the book includes analyses based on Sheldon's somatotyping scale and on a masculine-feminine body-build scale devised by the authors Unlike many previous twin studies, the authors have wisely included the variances of measurement errors (based on the differences between two measurements of the same dimension on a single person) Both the foreword (by Theodosius Dobzhansky) and the text emphasize the importance of learning more about polygenic inheritance in man and the fact that twins provide an excellent resource, not only for this purpose, but also for the equally important task of assaying the role of environmental factors in man, both in health and in disease Although the book does not quite reveal the "Genetic Basis of Morphological Variation," it does provide methodologic approaches for partitioning sources of human variation It will be an important reference for anyone planning a twin study and it may stimulate some readers to recognize the applicability of the twin study method to their own area of interest

C N Herndon, M D

QUESTIONS AND ANSWERS

HYPERPARATHYROIDISM

To the Editor —*Please advise me on the value of the various forms of phosphorus excretion tests compared to calcium balance studies in the diagnosis of hyperparathyroidism How is the phosphorus clearance test performed?*

Calixto A Romero, M D , Santurce, Puerto Rico

Answer —The current indirect methods of diagnosing hyperparathyroidism require demonstration of excess parathyroid hormone action on both calcium mobilization from bone and phosphate excretion by the kidneys Calcium balance studies are unnecessary Reproducible, reliable evidence of elevation of the serum calcium level suffices Hypercalciuria is of little diagnostic value Hyperphosphaturia is the rule in hyperparathyroidism and may be demonstrated by measurement of phosphate clearance or tubular reabsorption of phosphate (TRP) In either, urine is collected from a fasting, well-hydrated patient for four hours, e g , from 8 a m to 12 noon, and blood is drawn at the midpoint, e g , at 10 a m

$$PC = \frac{\text{UP (mg)}}{\text{SP (mg per 100 ml)} \times \text{T (min)}} \times 100$$

$$\%\ TRP = 1\frac{[UPC] \times [SCC]}{[UCC] \times [SPC]} \times 100$$

PC is phosphate clearance
UP is urine phosphate
SP is serum phosphate
TRP is tubular reabsorption of phosphate
UPC is urine phosphate concentration
SCC is serum creatinine concentration
UCC is urine creatinine concentration
SPC is serum phosphate concentration

TRP has the advantage of obviating errors in timing and such errors in collection as incomplete emptying of the bladder In hyperparathyroidism with normal or high dietary intake of phosphorus, phosphate clearance exceeds 15 ml per minute and TRP is less than 78%

Both these methods yield valuable diagnostic information, since parathyroid hormone accelerates phosphate excretion, i e , patients with hyperparathyroidism have increased urinary phosphorus excretion in relation to the low or low normal serum phosphorus levels, but neither method actually measures the physiological function involved The filtered phosphate load is overestimated, because about 15% of the serum inorganic phosphate is protein-bound and not filterable The clearance is, therefore, underestimated In addition, new data suggest excretion of phosphate by human renal tubules Empirical as they are, however, the tests are of value in demonstrating that the hypercalcemic patient also has hyperphosphaturia The combination of hypercalcemia and hyperphosphaturia occurs not only in hyperparathyroidism, but also in some cases of myeloma, sarcoidosis, vitamin D poisoning, and bronchogenic carcinoma which must, therefore, be excluded

DISCHARGE OF TUBERCULOUS PATIENTS

To the Editor —*What are the criteria for the discharge of a tuberculous patient from the sanatorium? Is a negative culture and result of animal inoculation test of gastric contents necessary? There seems to be a trend toward reducing the period of isolation if sputum tests are negative*

J W O'Neill, M D , White Cloud, Mich

Answer —Tuberculosis sanatoriums formerly tried to keep patients until the pulmonary lesion could be classified as "inactive" (i e , symptoms of tuberculous origin absent, lesions observed on serial roentgenograms stable except for extremely slow shrinkage, no roentgenographic evidence of cavity, sputum repeatedly negative on concentration test and also on culture or animal inoculation, and if patient is not raising sputum, fasting gastric contents or bronchial aspirates must be negative on culture or animal inoculation, all these conditions must exist for at least six months)

Since the advent of antituberculosis chemotherapy, there has been a trend toward much earlier discharge, with continuation of chemotherapy on an outpatient basis The time of discharge varies greatly in different institutions, depending on the availability of outpatient chemotherapy and other factors

Criteria for early discharge" have been published (Lichtenstein, *Am Rev Tuberc*, 74 961 [Dec] 1956) by the City of Chicago Municipal Tuberculosis Sanitarium Patients in a group designated as "active improved without cavity' are discharged when essentially asymptomatic, roentgenograms showing marked improvement (no demonstrable cavitation, and at least 50% clearing of infiltration), at least three consecutive 24-hour sputum concentrations negative for acid-fast bacilli, prognosis good, and living quarters suitable This group is discharged after an average of seven months of hospitalization The relapse rate in the first year is only 1%

Another group is designated "open-negative" (i. e, open cavity on roentgenogram and sputum negative) Patients in this group are eligible for discharge under the conditions given above, except that cavitation is still evident and roentgenograms should be stable for at least three months Note that the above criteria do not require that the patient's cultures be negative, although they usually are It is generally conceded that patients receiving chemotherapy who have repeatedly negative results of concentration tests are not a public health menace If positive on culture, they may, however, be dangerous to infants in the home

The open-negative group is discharged after an average of nine months of hospitalization The relapse rate is about 5% in the first year of outpatient care During the hospitalization period, every effort should be made to perform all indicated pulmonary surgery During outpatient chemotherapy, roentgenographic and sputum studies (including cultures) should be performed at appropriate intervals and rehospitalization should be available promptly if relapse occurs

WASP BITE

To the Editor —*A man was stung by two wasps on the face and neck Eight hours later he developed a temperature of 105 F (40 6 C) and became disoriented On admission to the hospital he was mentally confused He had purposeless muscular twitchings of the upper and lower extremities Results of the physical examination were essentially negative The leukocyte count on admission was 4700 per cubic millimeter, with lymphocytes predominating This rose to 14,000 on the next day, with polymorphonuclear cells predominating Results of the agglutination tests were all negative Spinal fluid findings were negative The patient was given 1 million units of penicillin and 500 mg of chloramphenicol four times a day On the seventh day, his temperature started to fall and his mentality started to improve He was afebrile and mentally clear by the 10th day Could this illness have been due to the wasp stings?*

A D Talusan, M D, Baltimore

Answer —Systemic reaction to the sting of wasps and other Hymenoptera may take the form of mental confusion and fever These may occur several hours later but usually last for only a few hours or at most several days This type of reaction is more often seen in children The questioner describes an unusually severe reaction to two stings Thorough studies failed to reveal any other basis for the clinical findings, yet delay of eight hours before the onset of symptoms, the height and duration of fever, and the neurological symptoms with recovery after antibiotic therapy make one wonder if the relationship of the stings to the subsequent symptoms was not fortuitous If, however, this patient has had unusual reactions from stings previously, it would be wise to test with wasp and other Hymenoptera antigens, if these reveal hypersensitivity, desensitization might be tried

The venom of wasps and other Hymenoptera has pharmacological actions similar to that of cobra venom The quantity from two stings, however, is usually insufficient for so severe an envenomation Kaszalka (*Bull U S Army M Dept* 9 212 [March] 1949) reported symptoms from envenomation involving several hundred stings Williams (*J South Carolina M A* 47 187 [June] 1951) reported a reaction with fever reaching 107 F (41 7 C) for several days beginning three hours after six or seven wasp stings

REFRACTIVE ERRORS

To the Editor —*Is it possible to correct myopia and hyperopia by injection of a substance into the aqueous or the vitreous humor, or both, which would alter the refractive index of either or both of these fluids?*

M D, Connecticut

Answer —Insertion of lenses into the anterior chamber to correct the refractive error of aphakia or myopia is the closest approach to alteration of the index of refraction of the vitreous or aqueous humor Since the aqueous and vitreous are being constantly renewed, it is difficult to envision any liquid compound which, after injection, would remain in position and not interfere with the physiology of the eye

STEATOCYSTOMA MULTIPLEX AND SPOON NAILS

To the Editor —*In the reply to the question regarding the concurrence of steatocystoma multiplex and spoon nails in* The Journal, *Feb 6, page 640, it was not mentioned that steatocystoma multiplex can be associated with multiple intestinal polyps Not only has an association between multiple sebaceous cysts and familial polyps been noted, but a relationship between such other soft tissue cutaneous tumors as fibromas, lipomas, and familial polyps has been noted as well A pertinent reference is that of Labarge and Mayo* (Proc Staff Meet Mayo Clin 32 749 *[Dec 25] 1957)*

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ABSTRACTS FROM THE LITERATURE

Archives of Pathology

70 1-124 (July) 1960

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A W Gottmann p 117

Liver in the Aging Process—Certain histologic changes in the aging liver have been previously described by other investigators This study re emphasizes these findings and defines other histological changes in livers of aged humans Sections of livers from 55 autopsy cases of sudden traumatic death without known previous liver disease were studied in respect to changes thought to be associated with normal aging Sections of livers from both young and old people were examined On the basis of this study marked variations in (1) parenchymal cell size (2) nuclear size and (3) nuclear staining characteristics are added to the list of known hepatic changes associated with the aging process [(1) giant parenchymal cells (2) giant, hyperchromatic, irregularly-shaped, aberrant nuclei in the parenchymal cells, (3) multiple nucleoli (5-15) within the giant nuclei (4) large, round or oval poorly stained, homogeneous-appearing inclusion bodies within the cell nuclei (not related to nuclear glycogen vacuolization) (5) binucleated cells, (6) clear perinuclear zone]

Carcinoma of Liver with Cirrhosis in Children—This study is a review of the literature with 1 case report There were 129 patients 8 of whom had concomitant cirrhosis 2 of these were adeno carcinoma and 6 were of liver cell type Cirrhosis with associated carcinoma of liver cell type in adults was 15%, and of adeno-carcinoma was 12-25% more common than in infants and children Cirrhosis was thought to have been congenital and thus an etiological factor in the production of carcinoma in many of these cases Ages ranged from 3 to 15 years in the patients with associated cirrhosis, 2 of these were below 4 years old The case reported is one of them Males were slightly preponderant

Lesions of Intramural Coronary Artery Branches—The frequency of inflammatory, fibrous or fibroelastic (hemodynamic) atheromatous, and proliferative lesions of the intramural coronary branches was compared in 116 diabetic and 105 non-diabetic patients who came to postmortem examination with severe coronary artery disease and myocardial infarction Inflammatory, hemodynamic and atheromatous lesions of the intramural coronary branches were found no more frequently among diabetics than among non-diabetics On the other hand, proliferative lesions of arterial branches of all size categories and of venules, as well as arteriolosclerotic-like lesions of small arteries and arterioles, were found from 2 to 2½ times more frequently among diabetics than among non-diabetics The proliferative lesions were characterized by a hyperplasia of endothelial cells, between which occurred a network of fine PAS-positive fibrils The arteriolosclerotic-like lesions showed only enlargement of endothelial cells without proliferation and several layers of fine PAS-positive fibrils in the wall The latter lesions were similar to those observed in placentas and in lower extremities, and previously reported as casually associated with diabetes

Stimulation of the Reticuloendothelial System—Intravenous injection of complete Freund s adjuvant (Mycobacterium butyricum) was used to stimulate the reticuloendothelial system in the rabbit There was a marked proliferation of the reticuloendothelial cells vascular endothelium, and interstitial connective tissue in a variety of organs The intensity and distribution of the lesions varied with dosage and time after the injection The cellular reaction was of a progressive type even with a single injection after a 4-week period There was a marked histiocytic response in the lung, frequently accompanied by a vasculitis There was an interstitial myocarditis which occasionally resembled Aschoff nodules Glomerular lesions resembling those reported in experimental glomerulonephritis were present There were nodular aggregates of reticuloendothelial cells (histiocytes) throughout the liver and spleen Some animals had vascular lesions similar to those found in serum sickness

Nuclear and Nucleolar Alterations in Hepatic Cells—Alterations in the form and function of hepatic cell nuclei during induction of cirrhosis in the choline deficient rat were studied karyometrically Within 1 week after beginning the dietary regimen, the total nucleolar volume and the ratio of nucleolar volume to nuclear volume of hepatic cells were increased Subsequently nuclei with greatly increased volumes appeared and formed an extension of the geometric series of nuclear volumes present in controls These changes are thought to represent a regenerative response of damaged liver They preceded the devolpment of actual nodular regeneration and cirrhosis by several months This study indicates that regeneration begins very early in the course of hepatic injury due to choline deficiency and long before the development of definite regenerative nodules

Oxytalan Fibers in Dental Granulomas and Radicular Cysts—The presence of oxytalan connective tissue fibers which are distinct from the collagenous reticular, and elastic varieties has been previously described in the normal periodontium of mice, rats guinea pigs and man During the development of dental granulomas and radicular cysts existing connective tissues and bone are destroyed at the apices of teeth, and new tissues are produced By using human formalin-fixed ileocecal valve are left intact, nutritional deficiency will be minimal Megaloblastic anemia developed in 5 of the 14 patients who underwent extensive resection with removal of the ileocecal valve The ileum was found to be more functional than the jejunum in relation to fat and vitamin B_{12} absorption Deficiency in nutritional state from extensive resection was treated with a high caloric diet, and megaloblastic anemia with oral and parenteral vitamin B_{12} and folic acid

Gazeta médica portuguesa, Lisbon

12 623-780 (Nov -Dec) 1959 Partial Index

Adrenalectomy and Ovariectomy in Breast Carcinoma
E G Amaral and L S Botelho p 647
Rare Case of Massive Pulmonary Ossification
J C Pimentel p 659

Rare Case of Massive Pulmonary Ossification—A 53-year-old man was hospitalized with fever, cough, and bloody sputum after being treated during 1 year for tuberculous pulmonary lesions Roentgenographic examination revealed retraction of the left hemithorax, where multiple cavitations were visible The patient improved under antibiotic medication, but the symptoms recurred At pneumonectomy a stony, orange-sized mass was found in the upper lobe of the right lung Section of the mass showed an ovoid cavity with osseous walls In a small segment at the upper part of the cavity the osseous tissue consisted of thin trabeculae Histological examination showed osseous trabeculae in contact with the external surface of the bronchial cartilages, sometimes imbedded in them In a small segment with almost no ossification, foci of fibrous connective tissue were limited by deposits of coal dust alternating with pulmonary parenchyma The findings in this case, which supposedly is the 8th in the literature, confirm the concept that massive pulmonary ossification is a definite anatomicoclinical entity, the onset of which presents itself under the form of acute bronchopneumonia that becomes chronic and resistant to antibiotic treatment The hypothesis that the ossification is secondary to a chronic pulmonary suppuration is presented

Irish Journal of Medical Science, Dublin

6 153-200 (April) 1960 Partial Index

Cystic Cavitation Following Chemotherapy of Tuberculosis
J T Cassidy and J D Kennedy p 153
Serum Proteins in Health and Disease
W E Bennett p 162

Cystic Cavitation Following Chemotherapy—Fifteen patients with cavitary tuberculosis were treated with isoniazid combined with other chemotherapeutic agents The tuberculous lesions cleared satisfactorily in all patients, but as they healed the formation of multiple, large thin-walled cysts was detected Many of the specimens obtained at pulmonary resection performed on 12 patients were free from tubercles, which indicates that the cysts may be regarded as complications of the chemotherapy Single or small cysts presented bronchiectatic complexes adjacent to their proximal margins, and gross communication with bronchi was found in 7 patients Older and stabilized specimens showed cavity walls composed of fibrous tissue less than a millimeter thick The incidence of cystic cavitation is attributed to the increased effectiveness of the combined therapy, which produced a more rapid resolution of tuberculous lesions, rather than to any specific action of isoniazid

Lancet, London

1 713-778 (April 2) 1960 Partial Index

Axillary Lymph Nodes Without Breast Carcinoma
T J McNair and H A F Dudley p 713
A Mongol Girl with 46 Chromosomes
P E Polani and others p 721
Chromosomal Abnormalities in Father and Mongol Child
F Fraccaro K Kaijser and J Lindsten p 724
Expired-air Resuscitation
J Cox, R Woolmer, and V Thomas p 727
Mucosa of Stomach and Intestine in Iron Deficiency
A Rawson and F D Rosenthal p 730

Axillary Lymph Nodes Without Breast Carcinoma—The authors feel that lack of knowledge about the clinical pattern of the axillary lymph nodes in "normal" women is surprising in view of the importance attached to the condition of these lymph nodes in judging the stage of breast carcinoma Investigations were carried out to ascertain (1) the percentage of normal women who have palpable axillary nodes, (2) the differences between the findings of different examiners In part 1 of the investigation 2 observers each examined the axillas of 62 patients who were in hospital for treatment of conditions not related to their breasts or axillas The finding of palpable nodes by the 2 observers was fairly uniform, but they disagreed on the presence or absence of nodes in 27% of axillas Five clinicians took part in the 2nd stage of the investigation on 10 patients Each patient was draped in such a way as to expose only the shoulders and axillae, the breasts were concealed as far as possible In 6 of these patients the breasts were normal and there was no reason for expecting the axillary nodes to be enlarged The other 4 had abnormalities of the breasts The results of this examination supported and magnified the findings of the 2 clinicians in part 1 The facts that emerged were (1) Palpable axillary lymph nodes were found in 37% of "normal" women, (2) clinicians differ on the presence or absence of palpable nodes in 35 to 40% of patients These findings raise doubts as to the value of the condition of lymph nodes as a means of judging the stage of breast carcinoma They emphasize that clinical premises require periodic re-examination, and that differences in clinical observation between examiners are commonplace

Neurology, Minneapolis

10 431-524 (May) 1960 Partial Index

Interaction of Viruses with Native Brain Substrates
S Bogoch p 439
Catecholamine Metabolism in Basal Ganglia Diseases
A Barbeau p 446
Central Nervous System in Congenital Heart Disease
M M Cohen p 452
Immunochemical Studies on Muscle Proteins
B Horvath and others p 457
Vestibular Disturbances in Epilepsy
B H Smith p 465
Metachromatic Form of Diffuse Cerebral Sclerosis
J H Austin p 470
Neurologic Aspects of Temporal Arteritis
R W Hollenhorst and others p 490

Neurologic Aspects of Temporal Arteritis—The authors have reported on 175 patients with temporal arteritis who were seen at the Mayo Clinic between 1931 and 1959 There were 95 women and 80 men Seven patients were aged from 50 to 59 years, and the rest were aged 60 years or older Some form of ocular involvement resulted from temporal arteritis in 102 patients, 73 patients (42%) had lost part or all of their vision permanently at the time of their discharge from the clinic, and 22 (12%) had diplopia Eighty eight patients were seen in consultation by a neurologist because of headaches, blindness, and other symptoms that often suggested the presence of an intracranial lesion The results of neurological examination were normal in 69 of the 88 patients, and abnormal in 19 If one excludes paresis of the ocular muscles, the incidence of objective neurological or electroencephalographic findings was exceedingly low the abnormalities that were present probably resulted from involvement of the intracranial arteries and the arteries coming off the aortic arch Treatment with cortisone or 1 of the other adrenocorticosteroids was practiced in 104 patients, and 17 of these patients received anticoagulant therapy also The remaining 71 patients were not treated or were treated with heparin, penicillin, or other substances before October 1949, when steroids were first employed Only 1 of the 104 patients lost vision after treatment with steroids was started Early therapy with adrenocortical steroids is urgently indicated and should not be delayed

New England Journal of Medicine, Boston

262 787-838 (April 21) 1960 Partial Index

Chloramphenicol in the Newborn Infant
C F Weiss and others p 787
Chronic Idiopathic Neutropenia
E A Browne and A J Marcus p 795
Peritoneal Dialysis in Boric Acid Poisoning
W E Segar p 798

Peritoneal Dialysis in Boric Acid Poisoning—Three infants with severe boric acid poisoning were treated with exchange transfusions followed by peritoneal dialysis There were 2 boys and 1 girl ranging in age from 3 to 6 days This experience provided an opportunity to compare the relative efficiency of these 2 procedures in effecting the removal of a water soluble toxin as well as to demonstrate the practicality of peritoneal dialysis in newborn infants Two of the infants had severe oliguria associated with jaundice, nervous hyperirritability, and erythema of large areas of the skin, 1 of these died on the 4th hospital day The 3rd infant, although symptomatic, was less seriously ill Peritoneal dialysis performed for 24 and 48 hours respectively gave excellent results in the 2 remaining infants, both of whom completely recovered Peritoneal dialysis was easily performed, the only complication encountered was leakage around the peritoneal catheter Four hours of peritoneal dialysis removed approximately the same amount of boric acid as could be removed by an exchange transfusion Continuous dialysis for 24 to 48 hours is, therefore, much more effective than exchange transfusion Peritoneal dialysis seems to be the treatment of choice for infants critically ill because of boric acid poisoning, and it should be considered in the treatment of poisoning caused by other water-soluble toxic substances

New Zealand Medical Journal, Wellington

59 123-176 (March) 1960 Partial Index

Intestinal Infarction Without Macroscopic Occlusions of Vessels
J B Blennerhassett and J D Reid p 131
Systemic Mast Cell Disease with Hereditary Spherocytosis
M McKellar and G F Hall p 151
Pseudo-Hypoparathyroidism Report of a Case
J K Laing p 156

Pseudo-Hypoparathyroidism—The 12-year-old boy whose history is presented had a history of tetany accompanied by low serum calcium and high inorganic phosphorus levels in the blood The condition was spontaneous, since the boy had not undergone thyroidectomy or other procedure which could have destroyed the parathyroids Because of the presence of calcification and bone formation in the skin this patient falls into the pseudo-hypoparathyroid group which was first described by Albright in 1942 and is regarded as showing these characteristics (1) brachydactylia, (2) a body habitus characterized by a round face and a thick-set figure (3) resistance to the action of parathyroid hormone, (4) demonstrable presence of parathyroid gland tissue, and (5) subcutaneous calcification or bone formation In addition to Albright s report, the author mentions other literature reports on pseudo-hypoparathyroidism, particularly that of Mowbray in 1954, who emphasized the existence of 3 genetic faults, namely a disturbance in the peripheral action of parathyroid hormone, a dyschondroplasia, and a tendency to subcutaneous calcification and bone formation The boy presented showed some resistance to dihydrotachysterol (A T 10) However, after treatment was begun, even with the apparently ineffective dihydrotachysterol, improvement became evident Tetany subsided, the Chvostek and Trousseau s signs became negative and the boy s parents felt that he had been benefitted and was more alert Resistance to the peripheral action of the parathyroid hormone was not proved, since the preparation used proved inactive in a normal control

Pediatrics, Springfield, Ill

25 737-906 (May) 1960 Partial Index

Antibiotics and Bacterial Meningitis
R J Haggerty and M Ziai p 742
Idiopathic Spontaneous Hypoglycemia in Children
J C Haworth and F J Coodin p 748
Syndrome of Recurrent (Cyclic) Vomiting
C S Hoyt and G B Stickler p 775
Mumps Virus Infection Simulating Paralytic Poliomyelitis
E H Lennette and others p 788

Antibiotics and Bacterial Meningitis—The authors report on 136 children with acute bacterial meningitis who were admitted to The Children s Hospital Medical Center in Boston, between 1956 and 1959 Of these, 65 received maximal doses of the single antimicrobial agent considered optimal for each causative organism, i e, chloramphenicol for Hemophilus influenzae, sulfadiazine for Neisseria meningitidis, and penicillin for Diplococcus pneumoniae The remaining 71 patients received multiple agents, i e, chloramphenicol, streptomycin, and sulfadiazine for H influenzae, sulfadiazine and penicillin for N meningitidis and penicillin and sulfadiazine for D pneumoniae Of 21 patients in whom the causative bacterial agent was unknown, 9 received single drug' therapy with chloramphenicol and 12 received multiple drug therapy with chloramphenicol and penicillin The patients who received multiple antibacterial drugs and those who received single antibacterial drugs were generally comparable There was no significant difference in the results, i e, neither synergism, antagonism, nor additive effects were observed, in this clinical study It seems reasonable to recommend that, in patients over 1 month of age with acute primary bacterial meningitis in whom a causative agent cannot be promptly identified, the administration of multiple drugs aimed at the 3 most likely organisms (D pneumoniae, N meningitidis, and H influenzae) can be employed without danger of clinically apparent antagonism

Syndrome of Recurrent (Cyclic) Vomiting—The authors report on 44 children who began to have recurrent vomiting before the age of 6 years, and who were seen at the Mayo

Clinic between 1945 and 1957 A questionnaire, which was mailed 2 to 14 years after the original examination to determine the prognosis and cause of the recurrent vomiting, was answered by 38 of the 44 patients or by their parents Thirty patients had no recurrent vomiting at the time of follow-up Of the remaining 8, there was less than a 5-year follow-up in 7 The average duration of the symptoms of episodic vomiting at the time of follow up of these 8 patients had not exceeded 8 years The cause of the syndrome of recurrent vomiting, while possibly psychogenic, is not known definitely It usually terminates before puberty There may be some relationship to migraine which also may be a syndrome and not a definite disease entity Electroencephalographic study of 15 of the patients did not suggest any relationship to a convulsive disorder

Mumps Virus Simulating Paralytic Poliomyelitis —The authors report on 11 boys, aged from 2½ to 8 years who were clinically considered to have mild paralytic poliomyelitis but in whom there was clearcut serologic evidence of mumps virus infection Poliomyelitis viruses were not isolated from the stools, and complement-fixing and neutralizing antibodies to poliomyelitis were either absent or did not significantly change in titer between the acute-phase specimens and the convalescent-phase specimens of serum Clinically, fever, headache, muscle pain, and slight to moderate weakness of several muscle groups were prominent manifestations The cerebrospinal fluid uniformly contained over 100 leukocytes, and commonly over 300, predominantly lymphocytes Only 2 of the 11 patients showed evidence of parotitis and in these parotitis did not antecede the manifestations of the central nervous system Electroencephalograms were made on 8 patients, and the recordings were abnormal in 3 All the 11 patients had evident muscle weakness at the end of the acute phase of illness, and 4 had slight residual weakness on convalescent examination 2 to 5 months after the onset of illness There was no significant predilection for any muscle group These observations emphasize that involvement of the central nervous system with the virus of mumps may be manifested as a syndrome of meningomyelitis and it may be erroneously diagnosed as paralytic poliomyelitis Weakness is usually highly transitory, but residual involvement may persist for some months As the incidence of paralytic poliomyelitis is reduced by widespread immunization, mumps virus may assume increasing relative importance as a cause of "poliomyelitis-like" disease

Presse médicale, Paris

68 675-714 (April 9) 1960 Partial Index

Herpangina Epidemic in Hospital Environment
J Gerbeaux and others p 675
Emergency Treatment of Suffocating Pneumothorax
G Hinaut J Felce, and B Muller p 681
Intracellular Development of "Reovirus"
P Tournier and M Plissier p 683

Herpangina Epidemic in Hospital Environment —An epidemic of herpangina affected the majority of 13 children (ages ranging from 19 to 41 months) in a tuberculosis ward Rhinopharyngeal manifestations (only typical features in the clinical picture) consisted of round, shining vesicles measuring 2 to 4 mm in diameter and turning into small ulcerations with a grayish coat A Coxsackie A-4 virus was isolated from rectal cultures from 6 children (4 with typical herpangina, 1 with congestive pharyngitis, and 1 with normal throat) Serologic study of antipoliomyelitic antibodies showed increase of the antibodies fixing the complement in 7 out of 9 patients, an increase in the antibodies neutralizing type 1 virus was found in 5 patients on whom the study was made Increase in the antibodies neutralizing the enteric cytopathogenic human orphan virus was found in 4 out of 11 patients The epidemic of herpangina was attributed to a Coxsackie A-4 virus, although 3 simultaneous infections were detected The risk of dissemination of infection in grouping children for medical treatment and the need for a control group for virologic identification of unusual clinical pictures are emphasized

Quarterly Journal of Medicine, London

29 1-152 (Jan) 1960 Partial Index

Primary Iron-Deficiency Anemia in Young Men
W Brumfitt p 1
The Marfan Syndrome
R J G Sinclair, A H Kitchin, and R W D Turner p 19
Hodgkin s Disease With and Without Alcohol-Induced Pain
A H James p 47
Surgical Treatment of Internal Carotid Artery Occlusion
C H Edwards N S Gordon and C Rob p 67
Ocular Changes in Graves' Disease
I B Hales and F F Rundle p 113
Gout, Familial Hyperuricemia and Renal Disease
H Duncan and A St J Dixon p 127

Primary Iron-Deficiency Anemia —The author carried out a survey of hemoglobin levels among 2,000 recruits of the Royal Army Medical Corps Iron-deficiency anemia not associated with organic disease was found in 1 1% of these recruits Details are given of the findings in 30 men, 18 or 19 years of age, with iron-deficiency anemia in whom exhaustive studies failed to reveal organic disease When seen 3 to 12 months after correction of the anemia by oral administration of iron, none of the patients had relapsed Acid had returned to the gastric secretion in many of those who previously had achlorhydria It is clear that, if primary iron-deficiency anemia were to develop in men, the most likely time would be between the ages of 18 and 20 years, when they are completing a period during which the iron requirement is increased The incidence of anemia of only 1 1% among recruits suggests that these men must have some basic defect which determines that they will become anemic It seems likely that the young men in whom primary iron-deficiency anemia develops are those whose iron uptake from food is relatively poor It is possible that most of these men recover spontaneously when growth ceases and iron requirement is reduced to a level at which the amount of iron absorbed from the diet is sufficient to restore the iron content of the body gradually to normal Primary iron deficiency in young men leads to a state of chronic ill health and loss of efficiency at a critical time in the patient's career Wider recognition of the condition would lead to early detection and treatment of the illness

Marfan Syndrome —The authors describe the skeletal and cardiovascular manifestations of Marfan syndrome in 40 patients, 14 of whom had both skeletal and cardiovascular changes With regard to musculoskeletal manifestations it is suggested that the term arachnodactyly should be reserved for patients with long, thin fingers, and with a metacarpal index greater than 8 4, based on the roentgenographic appearance of the hand Should such a patient also have a span of the outstretched arms exceeding the height by more than 3 in (8 cm), together with a lower segment (pubis to heels) greater than the upper segment (pubis to vertex) by more than 2 in (5 cm), the diagnosis of Marfan syn drome should be considered The relative importance of the skeletal manifestations and the frequency with which symptoms due to the syndrome are unrecognized as such have been discussed Of the cardiovascular anomalies which have been observed in association with skeletal or ocular manifestations of the syndrome, dilatation of the aortic valve ring, the sinuses of Valsalva the aortic arch or descending aorta or rupture of the aorta with or without a dissecting aneurysm, may result from medionecrosis Dilatation of the pulmonary artery may also result from medionecrosis Deformities of the valve cusps, with cardiac murmurs, may result from myxomatous degeneration Myocarditis, defects of conduction, and cardiac arrhythmia may occur, but the pathogenesis is obscure Rheumatic heart disease may occur, but more often valvular defects result from myxomatous degeneration Atrial septal defect, coarctation of the aorta, and patent ductus arteriosus may be present and are probably associated congenital defects rather than etiologically part of the syndrome

Hodgkin's Disease and Alcohol—A clinical and histological comparison was made of 13 patients with Hodgkin's disease who had been admitted to the Royal Infirmary or Radiotherapy Center in Cardiff, England, and who had had pain after almost all kinds of alcoholic drink in at least 1 of the sites of the disease, with 20 patients who had not had alcohol induced pain The histological comparison based on lymph node biopsy was made independently by 3 observers who were ignorant of the histories of the individual patients All 3 found fewer reticulum-cell mitoses, more eosinophil cells, and more fibrosis in sections from patients who had had alcohol-induced pain The patients with alcohol-induced pain had much more often at the time of biopsy spontaneous pain, mediastinal involvement, and a leukocytosis than those patients who did not have alcohol-induced pain After discussion of possible causes of the pathological and clinical differences found, it is suggested that Hodkgin's disease with alcohol-induced pain is a separate entity A review of the literature relating to alcohol-induced pain revealed that of 27 patients with alcohol-induced pain whose sex was given 14 were men and 13 were women The sex incidence of this condition, thus does not favour men, in contrast with Hodgkin's disease as a whole

Radiology, Syracuse, N Y

74 529-704 (April) 1960 Partial Index

Cellular Aspects of Tumor Therapy
M M Elkind p 529
Pulmonary Veins in Rheumatic Heart Disease
R S Ormond and A K Poznanski p 542
Cinefluorographic Detection of Calcifications in Heart
J Jorgens and others p 550
Aortic Configuration in Congenital Heart Disease
E C Klatte and others p 555
Papillary Opacification in Excretory Urography
F G Fleischner and others p 567
Gastrointestinal Carcinoid Tumors Roentgen Features
I Bluth p 573
Simple Distal Ileal Obstruction
B S Epstein p 581

Aortic Configuration in Congenital Heart Disease—The usefulness of aortic configuration in the diagnosis of congenital heart disease was evaluated by reviewing angiocardiograms of 610 patients exhibiting 12 commonly encountered cardiac lesions The aorta was enlarged in tetralogy of Fallot, tricuspid atresia without transposition, truncus arteriosus type 4, aortic stenosis, patent ductus arteriosus aortic stenosis, and coarctation In the latter 3 conditions the aortic configuration was sometimes sufficiently characteristic to permit roentgen identification The large aorta of tetralogy of Fallot served to distinguish this condition from pulmonary stenosis with right-to-left interatrial shunt, where the aorta was usually small The large aorta was a useful sign in differentiating tricuspid atresia from tricuspid atresia associated with transposition of the great vessels, where the aorta was small The aorta was decreased in size in atrial septic defects, anomalous pulmonary venous return, truncus arteriosus types 1, 2, and 3, pulmonary stenosis, tricuspid atresia with transposition, transposition of the great vessels, and fibroelastosis Specific aortic contour was as reliable a diagnostic sign of coarctation of the aorta as was rib notching This is of practical value because 1 sign may be present when the other is absent

Gastrointestinal Carcinoid Tumors—The author reviewed the records of 509 patients with carcinoid tumors of the gastrointestinal tract He points out the signs of the malignant carcinoid syndrome consisting of chronic diarrhea, respiratory distress, right-sided cardiac disease, flushing and cyanosis All gastrointestinal carcinoids except those of the appendix should be considered malignant Carcinoid tumors differ from other malignant neoplasms by the long duration of the disease Carcinoids occurred in the appendix, stomach, duodenum, jejunum, colon and rectum but the usual site was in the ileum within a few feet of the ileocecal valve It is in this location that carcinoids most frequently metastasize and eventually lead to the carcinoid syndrome Appendical and rectal carcinoids were not of radiological significance The chief roentgen findings for the carcinoids of other sites were a polypoid mass and some degree of obstruction Four patients with gastrointestinal carcinoid tumors are reported In 1 of these the tumor was intraluminal, widening the caliber of the involved ileal segment This represents an unusual growth pattern since the growth is usually in the direction of the serosa

Revista clínica española, Madrid

76 79 144 (Jan 31) 1960 Partial Index

Fat Absorption in Adrenolectomized Animals
J M Linazasoro and C J Diaz p 87
Hypothermia with Extracorporeal Circulation
E G Ortiz p 92
Hemostatic Value of Hemocoagulase
T S Alonso and F G López p 103

Hemostatic Value of Hemocoagulase—Hemocoagulase (Reptilase), an enzyme from the venom of a Brazilian snake (Bothrops jararaca) was used in 2 series of patients The 1st series comprised 20 patients with different types of otorhinolaryngologic disease and constituted an experimental group Coagulation time was determined in vitro at intervals of ½ hour, 2 hours and 24 hours after an intramuscular injection of hemocoagulase The maximal coagulating effect was reached within 3 hours and persisted for 24 hours in 88% of the patients The 2nd series comprised more than 100 patients, adults and children, who underwent tonsillectomy Each patient received 1 Klobusitzky unit of hemocoagulase intramuscularly, 1 hour before the operation Calcium, vitamin C, and P factors were also given The loss of blood was minimal, hemorrhage occurred in only 2 patients who had recurrent phlegmonous tonsillitis Good results were also obtained in laryngofissures partial laryngectomy, ear operations, and treatment of epistaxis The authors believe that the preoperative administration of hemocoagulase is useful for normal surgical patients and indispensable for those with a delayed blood coagulation

Rev españ. oto-neuro-oftal., Valencia

19 1-72 (Jan -Feb) 1960 Partial Index

Pateencephalographs in Diagnosis of Meningiomas
J J Barcia-Coyanes and J L Barcia Salorio p 1
Dihydrochlorothiazide in Endolymphatic Hydrops
M C Juan R L Martinez, and J M Clemente p 8
Surgical Treatment of Parkinson's Disease
M B Valls p 30

Surgical Treatment of Parkinson's Disease —Twenty-six patients were treated surgically by 4 different techniques (1) Pallidectomy with destruction of the globus pallidum by alcohol was performed on 5 patients Immediate results were satisfactory, with cessation of tremor and decrease of rigidity One patient went into irreversible coma 48 hours after the operation Postoperative contralateral facial hemiparesis persisted in 1 (2) Electrocoagulation was performed on 3 patients The postoperative period was complicated by fever and cerebral edema in 2 patients, 1 of whom died The 2 surviving patients obtained permanent improvement (3) Destruction of globus pallidum with leukotome was performed on 5 patients, of whom 1 died during the operation Immediate results were satisfactory in the others (4) Destruction of globus pallidum by combined cutting and injection of boiling water was performed on 19 patients With the exception of 1 patient, permanent improvement was obtained Pallidectomy with injection of boiling water is considered safer than, and as effective as, the other techniques described

Thoraxchirurgie, Stuttgart

7 547-642 (April) 1960 Partial Index

Pulmonary Sequestration Clinical Importance
F Baumgartl and H Gremmel p 547
Bronchitis Deformans in Pulmonary Tuberculosis
W Reichmann and W Kuhne p 559
Isolated Middle Lobe Processes A Syndrome?
W Schramm p 584
Congenital Pulmonary Emphysema and Tension Cysts in Infants
R X Zittel p 594
Cartilage Resections in Progressive Necrosis of Rib Cartilages
G Borger p 612

Pulmonary Sequestration —A pulmonary sequestration is not connected with the regular bronchial system and it is supplied by atypical vessels It may be located within or outside of the lung The condition has been referred to as Rokitansky's lobe, intralobar sequestration, accessory lung, aberrant lobe, or abdominal lung On the other hand, the term sequestration has been applied to portions of the lung sequestrated as the result of septic or aseptic necrosis After commenting on the localization of the sequestrations, the behavior of the atypical vessels that supply them, the symptoms, diagnosis, and therapy on the basis of literature reports, the authors present 6 patients with this defect who were observed at the Surgical Clinic of the Medical Academy in Dusseldorf, over a period of 10 years in the course of 2,400 pulmonary operations The ages of the 6 patients ranged from 15 months to 38 years In the 2 children (15 months and 3 years) the pulmonary sequestration was associated with diaphragmatic hernia One patient, a 24-year-old man, had cystic degeneration of the entire lung on the side on which the sequestration was located The other 3 patients had only pulmonary sequestration Cure was obtained in all 6 patients, in 1 by pneumonectomy (cystic lung), in 2 by lobectomy, and in 3 by extirpation of the sequestration In studying the surgical reports of patients with pulmonary abscesses, the authors gained the impression that in some in whom the separation of adhesions to the posterior thoracic wall caused severe hemorrhages the abscess might have been caused by sequestration

Isolated Middle Lobe Processes A Syndrome?—Numerous reports have appeared about the middle lobe syndrome, but it has also been pointed out that this concept should be done away with, because it interferes with causal diagnosis The authors present observations on 10 patients who had isolated lesions of the middle lobe The symptoms were not uniform Roentgenoscopy of the middle lobe revealed in 6 cases atelectasis, in 2 a shadow, in 1 a round focus, and in 1 a cyst Therapy consisted of lobectomy in 6 cases, 1 patient was subjected to roentgen irradiation, surgery being inadvisable because of poor general condition, in another patient surgery was rejected because of lymphatic leukemia, and 2 patients recovered with conservative therapy Of the 6 patients with atelectasis 1 had a peripheral adenoma, 1 had carcinoma in the middle lobe bronchus, and another carcinoma of the intermediate bronchus, 1 had an acino nodular tuberculosis, 1 had calcified lymph nodes, and 1 bronchiectasis A shadow of the middle lobe was caused in 1 patient by an eosinophilic infiltration In 1 patient the middle lobe contained a solitary metastasis from a rectal carcinoma The round focus was of obscure etiology, and disappeared spontaneously Enlargement of the lymph nodes was observed at operation in 4 of the 6 cases subjected to lobectomy The cause of the enlargement was different in each case In 1 case it could have been due to hyperplasia of leukemic lymph nodes, but bronchoscopy disclosed carcinoma This case convinced the authors that the concept of the middle lobe syndrome should be given up Even when the swelling of the lymph nodes seems to be non specific, its cause should be searched for, so that the treatment can be directed against the cause

Congenital Pulmonary Emphysema and Tension Cysts —Acute respiratory insufficiency in newborn infants can have various causes, the identification of which may be difficult, but may prove of vital importance not only to preserve the life of the infant, but also with regard to complications and to definitive cure In this report the author is concerned with 2 possible causes, which, while rare, are usually not correctly identified and consequently do not receive the required surgical treatment The 1st of the 2 is congenital localized emphysema of the lungs This condition has been discussed repeatedly in the Anglo-American literature under such terms as congenital lobar emphysema, tension emphysema, localized hypertrophic emphysema, or lobar obstructive emphysema In discussions on the etiology, a congenital dysplasia of the lungs or of the bronchial system was generally mentioned The upper lobes are chiefly involved Additional developmental defects have been described In a case observed by the author such a defect consisted in a mediastinal hernia The tension cysts of the lung that cause respiratory insufficiency in infants are congenital cysts with epithelial lining They are connected with the bronchial system and, like the localized emphysema, are usually located in the upper pulmonary lobes After presenting a case history, the author discusses the diagnosis and the differential diagnosis Surgery is the only effective treatment for both these congenital defects The author warns against exploratory puncture

WASHINGTON NEWS

Republican Health Platform
Polio
Miscellany

HEALTH PLANK APPROVED BY GOP

The Republican Party approved a platform plank on health care for the aged along the lines of the program submitted by the Administration to Congress several months ago

The program does not embody the Social Security approach of the Democratic platform, which both President Eisenhower and Vice-president Nixon have repeatedly assailed as compulsory government medicine

However, the plank apparently is similar to the Administration s proposal for a voluntary plan of health insurance that needy oldsters might secure The House-passed health bill now before the Senate Finance Committee avoids the insurance concept and instead provides a program by which the federal and state governments would finance the costs of illnesses for medically indigent persons The American Medical Association has endorsed this program as best fitted to help those elderly persons who really need assistance in meeting their health bills

The clash between the two planks is likely to be settled when Congress reconvenes soon to finish its business for the year The House-passed bill on health care for the aged is before the Senate Finance Committee, which is expected to act soon on the legislation

Despite the GOP convention s action, the Administration plan still appears to lag behind the House measure and the sweeping Democratic Social Security plans as far as support in Congress is concerned Senate and House Republicans have criticized the Administration s bill as too costly and 'unworkable

Basically, the Administration plan would provide an insurance program for persons over 65 who have incomes less than a certain amount Deductible features would require such persons (not those on the public assistance rolls whose medical care is entirely free now) to pay a portion of the cost

Following is the entire health plank approved by the Republican Convention in Chicago

Human Needs

The ultimate objectives of our free society and of an ever growing economy are to enable the individual to pursue a life of dignity and to develop his own capacities to his maximum potential

Government's primary role is to help provide the environment within which the individual can seek his own goals In some areas this requires federal action to supplement individual, local, and state initiative The Republican Party has acted and will act decisively, compassionately, and with deep human understanding in approaching such problems as those of the aged, the infirm, the mentally ill, and the needy

This is demonstrated by the significant increase in social security coverage and benefits as a result of recommendations made by the Eisenhower-Nixon Administration As a result of these recommendations and normal growth, 14 million persons are receiving benefits today compared to five million in 1952, and benefit payments total $10 3 billion as compared to $2 5 billion in 1952 In addition, there have been increases in payments to those on public assistance, both for their basic needs and for their health and medical care, and a broad expansion of our federal-state program for restoring disabled persons to useful lives—an expansion which has accomplished the rehabilitation of over half a million persons during this Administration

New needs, however, are constantly arising in our highly complex, interdependent, and urbanized society

To meet the needs of the aging, we pledge

Expansion of coverage, and liberalization of selected social security benefits on a basis which would maintain the fiscal integrity of the system

Support of federal-state grant programs to improve health, welfare, and rehabilitation services for the handicapped older persons and to improve standards of nursing home care and care and treatment facilities for the chronically and mentally ill

Federal leadership to encourage policies that will make retirement at a fixed age voluntary and not compulsory

Support of programs that will persuade and encourage the nation to utilize fully the skills, wisdom, and experience of older citizens

Prompt consideration of recommendations by the White House Conference on Aging called by the President for January 1961

Health Aid

Development of a health program that will provide the aged needing it, on a sound fiscal basis and through a contributory system, protection against burdensome costs of health care Such a program should provide the beneficiaries with the option of purchasing private health insurance—a vital distinction between our approach and Democratic proposals in that it would encourage com-

(Continued on next page)

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr F J L Blasingame, 535 North Dearborn St, Chicago 10, Executive Vice-President
1960 Clinical Meeting, Washington, D C, Nov 28-Dec 1
1961 Annual Meeting, New York City, June 26-30
1961 Clinical Meeting, Denver, Nov 27-30
1962 Annual Meeting, Chicago, June 11-15
1962 Clinical Meeting, Los Angeles, Nov 26-29
1963 Annual Meeting, Atlantic City

AMERICAN

1960

August

American Association of Blood Banks, Jack Tar Hotel San Francisco Aug 21-26 For information write AABB Central Office, Suite 1619, 30 N Michigan, Chicago 2

American Congress of Physical Medicine and Rehabilitation, Mayflower Hotel, Washington D C, Aug 21-26 Mrs Dorothea C Augustin 30 N Michigan Ave Chicago 2 Executive Secretary

American Hospital Association, Civic Auditorium, San Francisco Aug 27-Sept 1 Mr Maurice J Norby, 840 N Lake Shore Dr, Chicago 11, Secretary

American Institute of Ultrasonics in Medicine, Statler-Hilton Hotel Washington, D C, Aug 20 Dr Dorothy M Stillwell Dept of Phys Med and Rehab, Univ of Colorado Med Center Denver 20 Chairman

American Physiological Society Stanford University Calif, Aug 22-26 Mr Ray G Daggs, 9650 Wisconsin Ave, Washington 14, D C Executive Secretary

American Society of Clinical Hypnosis Miami, Fla, Aug 7-10 Dr Seymour Hershman, 6770 N Lincoln Ave Chicago 46, Secretary

American Society for Pharmacology and Experimental Therapeutics, University of Washington, Seattle, Aug 21-25 Dr Karl H Beyer Merck Sharp & Dohme Research Laboratories, West Point Pa, Secretary

American Veterinary Medical Association, Denver-Hilton Hotel Denver Aug 15-18 H E Kingman Jr 600 S Michigan Avenue, Chicago 5 Executive Secretary

Biological Photographic Association, Inc, Utah Motor Lodge Salt Lake City, Utah, Aug 23-26 Miss Jane H Waters, Box 1668, Grand Central P O, New York 17 Executive Secretary

Conference on the Chemical Organization of Cells Normal and Abnormal University of Wisconsin Madison, Aug 25-27 Dr J F A McManus, Dept of Pathology, University of Alabama Medical Center, Birmingham, Chairman

Gerontological Society, Inc Mark Hopkins Hotel, San Francisco Aug 7-12 Mrs Marjorie Adler 660 S Kingshighway Blvd, St Louis 10 Administrative Secretary

National Medical Association Inc, Penn-Sheraton Hotel, Pittsburgh Aug 8-11 Dr John T Givens 1108 Church St Norfolk Va, Executive Secretary

Reno Surgical Society Mapes Hotel, Reno, Nev Aug 18-20 Dr Gilbert G Lenz, 505 S Arlington Ave, Reno, Nevada

Rocky Mountain Radiological Society Denver-Hilton Hotel Denver, Aug 11-13 Dr John H Freed 4200 E 9th Ave Denver 20, Secretary-Treasurer

West Virginia State Medical Association, The Greenbrier White Sulphur Springs Aug 25-27 Mr Charles Lively Box 1031, Charleston 24, W Va Executive Secretary

September

American Academy of Pediatrics, and American Academy of General Practice, Louisiana Chapter, Roosevelt Hotel New Orleans, Sept 23 Dr Herbert B Rothschild, 1520 Louisiana Ave, New Orleans 15, Chairman of Publicity Committee

American Association for Automotive Medicine Dearborn Inn, Dearborn, Mich Sept 19-20 For information write Dr H A Fenner Jr 115 W Sanger St Hobbs N M

American Medical Writers Association, Hotel Morrison, Chicago, Sept 30-Oct 1 Dr Harold Swanberg, 510 Maine St, Quincy Ill, Secretary

American Roentgen Ray Society Ambassador Hotel, Atlantic City Sept 27-30 Mr Hugh Jones, 20 N Wacker Dr, Chicago 6, Director Public Relations

American Society of Clinical Pathologists, Palmer House Chicago Sept 24-Oct 2 Mr Claude E Wells, 445 Lake Shore Drive, Chicago 11, Executive Secretary

College of American Pathologists, Palmer House, Chicago, Sept 24-27 Dr Arthur H Dearing, 2115 Prudential Plaza, Chicago, Executive Director

Colorado State Medical Society, Stanley Hotel, Estes Park Sept 14-17 Mr Harvey T Sethman, 835 Republic Bldg, Denver 2, Executive Secretary

Delaware, Medical Society of, Rehoboth Del, Sept Mr Lawrence C Morris Jr, 1925 Lovering Ave, Wilmington 6, Del, Executive Secretary

Flying Physicians Association third clinical meeting, Western Hills Lodge, Wagoner, Okla, Sept 6-9 For information write Flying Physicians Association National Headquarters, P O Box 3275, Tulsa Okla

Inter-Society Cytology Council, Palmer House, Chicago, Sept 23-25 Dr Paul A Younge 1101 Beacon St, Brookline 46, Mass, Secretary

Kentucky State Medical Association, Louisville, Sept 20-22 Mr J P Sanford, 1169 Eastern Parkway, Louisville 17, Ky, Executive Secretary

Maryland, Medical and Chirurgical Faculty of the State of Semiannual Meeting Ocean City, Sept 16 Mr John Sargeant, 1211 Cathedral St, Baltimore 1, Executive Secretary

Michigan State Medical Society Detroit, week of Sept 25 Dr D Bruce Wiley, 606 Townsend St, Lansing 15 Mich, Secretary

Montana Medical Association, Baxter Hotel, Bozeman, Sept. 15-1 Dr William E Harris, 114 N Second, Livingston, Montana, Secreta

National Cancer Conference, American Cancer Society, Inc., and the National Cancer Institute, Minneapolis Minnesota, Sept. 13-15 Dr Roald M Grant, 521 W 57th St, New York 19 Coordinat

National Recreation Congress Shoreham Hotel, Washington, D C. Sept 25-29 Willard B Stone 8 W Eighth St New York 11, Secretary

Nevada State Medical Association, Stardust Hotel, Las Vegas Sept. 7-10 Mr Nelson B Neff, P O Box 2790, Reno Nev Execu Secretary

New England Society of Anesthesiologists Bretton Woods N H Sept 18-19 Dr Thomas K Burnap, P O Box 81, Kenmore Station P O, Boston 15

Oregon State Medical Society, Portland, Sept 7-9 Mr Roscoe K Miller 2164 S W Park Place, Portland 5, Ore, Executive Secretary

Pacific Dermatologic Association Empress Hotel, Victoria, British Columbia Canada, Sept 1-4 Dr Edward J Ringrose 2636 Telegraph Ave Berkeley 4, Calif, Secretary-Treasurer

Society for Pediatric Radiology Ambassador Hotel Atlantic City N J, Sept 26 Dr Richard G Lester 412 Union St, S E Minneapolis 14 Minn, Secretary-Treasurer

Southern Trudeau Society (and Southern Tuberculosis Conference), Hotel Francis Marion, Charleston S C Sept 14 16 M Judson M Allred Jr P O Box 9865, Northside Station, Jackson Miss Secretary-Treasurer

Tennessee Valley Medical Assembly Read House Chattanooga Tenn. Sept 26-27 Dr Robert A Waters 109 Medical Arts Bldg, Chattanooga Chairman

Tri-State Medical Assembly, Captain Shreve Hotel Shreveport La. Sept 14-15 Dr J W Wilson Jr, 940 Margaret Place, Shreveport La, Secretary-Treasurer

Utah State Medical Association Hotel Utah Motor Lodge, Salt Lake City Sept 20-23 Mr Harold Bowman 42 S 5th East, Salt Lake City 2 Executive Secretary

Washington State Medical Association, Seattle Sept 25 28 Mr Ralph W Neill, 1309 Seventh Ave, Seattle 1, Executive Secretary

Wyoming State Medical Society, Jackson Lake Lodge, Moran Sept. 7-10 Mr Arthur R Abbey P O Box 2036 Cheyenne Wyo, Executive Secretary

October

Academy of Psychosomatic Medicine, Benjamin Franklin Hotel, Philadelphia, Oct 13-15 For information write Dr Bertram B Moss 55 E Washington, Chicago 2

American Academy for Cerebral Palsy Penn-Sheraton Hotel Pittsburgh, Oct 5-8 Dr Joseph D Russ, 1520 Louisiana Ave New Orleans 15, Executive Secretary

American Academy of Ophthalmology & Otolaryngology, Palmer House Chicago Oct 9-14 Dr William L Benedict, 15 Second St, S W, Rochester Minn, Executive Secretary

American Academy of Pediatrics, Palmer House Chicago Oct 17 20 Dr E H Christopherson 1801 Hinman Ave Evanston, Ill, Executive Director

American Association of Medical Clinics, New Orleans Oct 6 8 Dr Joseph B Davis, 134 N Washington St Marion Ind Secretary

American Association of Medical Record Librarians Olympic Hotel Seattle, Oct 10-13 Miss Doris Gleason 840 N Lake Shore Dr, Chicago 11 Executive Director

American Association of Poison Control Centers, Palmer House Chicago, Oct 18 Dr Harry C Shirkey 712 S 30th St, Birmingham Ala, Chairman, Program Committee

American Association for the Surgery of Trauma Coronado Hotel Coronado, Calif, Oct 5-7 Dr William T Fitts Jr, 3400 Spruce St Philadelphia 4, Secretary

American College of Gastroenterology, Bellevue-Stratford Hotel Philadelphia, Oct 23-26 Mr Daniel Weiss, 33 W 60th St, New York 23, Executive Director

American College of Surgeons, Clinical Congress, San Francisco Oct 10-14 For information write Dr William E Adams, 40 E Erie St, Chicago 11

American Fracture Association, El Presidente Hotel Mexico D F Mexico, Oct 30-Nov 4 Dr H W Wellmerling, 610 Griesheim Bldg Bloomington, Ill, Executive Secretary

American Heart Association, Inc Jefferson Hotel, St Louis Oct 21-25 Mr Rome A Betts, 44 E 23rd St New York 10, Executive Director

American Otorhinologic Society for Plastic Surgery, Inc, Conrad Hilton Chicago, Oct 9 Dr Joseph G Gilbert 75 Barberry Lane Roslyn Heights, L I New York Secretary

American Public Health Association, San Francisco Oct 30 Nov 4 Dr Berwyn F Mattison, 1790 Broadway, New York 19, Executive Director

American Rhinologic Society Belmont Hotel, Chicago, Oct 8 Dr Robert M Hansen, 1735 N Wheeler Ave, Portland 17, Ore, Secretary

American School Health Association, San Francisco Oct 30 Nov 4 Dr A O DeWeese 515 E Main St, Kent, Ohio Executive Secretary

American Society of Anesthesiologists, Inc, Statler Hilton New York City Oct 2-7 Mr John W Andes, 515 Busse Hwy Park Ridge Ill, Executive Secretary

American Society of Facial Plastic Surgery Chicago, Oct 13 Dr Samuel M Bloom, 123 E 83d St, New York 28, Secretary

American Society of Plastic and Reconstructive Surgery, Statler Hotel, Los Angeles, Oct 2-7 Dr Thomas R Broadbent 508 E S Temple, Salt Lake City, Secretary

Association of American Medical Colleges Diplomat Hotel, Hollywood Beach Fla, Oct 31-Nov 2 Dr Ward Darley, 2530 Ridge Ave, Evanston, Ill, Executive Director

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LIVE, ORALLY GIVEN POLIOVIRUS VACCINE

EFFECTS OF RAPID MASS IMMUNIZATION ON POPULATION UNDER CONDITIONS OF MASSIVE ENTERIC INFECTION WITH OTHER VIRUSES

Albert B Sabin, M D , Cincinnati, Manuel Ramos-Alvarez, M D , Jose Alvarez-Amezquita, M D , Mexico, D F , William Pelon, Ph D , Richard H Michaels, M D , Ilya Spigland, M D , Meinrad A Koch, M D , Joan M Barnes, Ph D
and
Johng S Rhim, M D , Cincinnati

The phenomenon of viral interference must be taken into account in planning the use of live poliovirus vaccine in areas where conditions favor the extensive dissemination of naturally occurring polioviruses Experience with feeding a trivalent vaccine to 26,033 children in a tropical city of 100,000 population led to the conclusion that interference was overcome by mass feeding of vaccine to 86% of all children under 11 years within a period of about four days, and that, because dissemination of the polio virus was self limited, a second feeding of trivalent vaccine was necessary to achieve immunization of almost all children Recommendations are here formulated for the eradication of poliomyelitis, but they apply only to subtropical and tropical regions with extensive dissemination of various enteric viruses and not to temperate zones with good sanitation and hygiene during certain periods of the year and under conditions of low or absent dissemination of enteric viruses

IN THE absence of enteric infection with other viruses, the feeding of a single type of live poliovirus vaccine to children who have not previously been infected with the same type of poliovirus usually results in viral multiplication in the intestinal tract, antibody formation, and complete or partial resistance to reinfection The use of live poliovirus vaccine in areas with climatic and hygienic conditions which permit extensive dissemination of naturally occurring polioviruses and other enteric viruses throughout the year has been complicated by the problem of viral interference,[1] which we have attempted to overcome by the tactics to be described in this communication

The studies of one of us (M R -A) and associates[2] in Mexico and of Plotkin and Koprowski[3] in the Belgian Congo have shown that vaccination programs in large subtropical or tropical cities that are spread out over a period of many weeks and include only a small fraction of the susceptible population not only fail to immunize a considerable proportion of the vaccinated children but also have little or no influence on the dissemination of the ever-present, naturally occurring paralytogenic strains of poliovirus Accordingly, it seemed necessary to determine whether at least temporary dominance over the naturally occurring polioviruses and other

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From the Children's Hospital Research Foundation University of Cincinnati College of Medicine Hospital Infantil Mexico D F and the Ministry of Health Mexico

Read in part before the 73rd annual meeting of the Association of American Physicians Atlantic City May 3 1960 interfering enteric viruses could be achieved by feeding a mixture of all three types of poliovirus vaccine to almost all susceptible children within a period of a few days The reason for using a trivalent mixture instead of feeding the three types separately at intervals of four to six weeks, which is regarded as optimum during the cold months of the year in temperate zones, was to implant all three types of the vaccine strains in the largest number of children and then let nature help in their further dissemination in the community

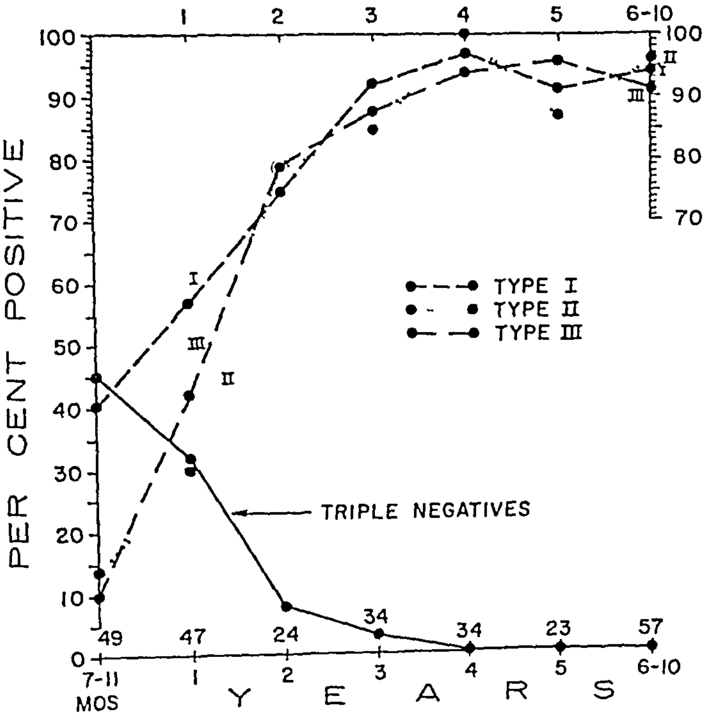


Fig 1 —Poliovirus antibodies in children in Toluca, Mexico, just before feeding vaccine Numbers above age groups indicate number of persons in each group tested

Methods of Study and Results

This study was carried out in Toluca, Mexico, in August, 1959 One of us (M R -A) and his associates in Mexico were responsible for the field work and the collection of specimens, and all the virological and serologic work was carried out in Cincinnati Toluca, located at a latitude of about 19 degrees north, has a total population of about 100,000 A serologic survey of the population just before initiation of the vaccine program indicated that 90 to 100% of the children become immune to all three types of poliovirus during the first 4 years of life (fig 1) According to available data for the past five years, this city has been paying an average price of 14 paralytic cases per year for this naturally acquired immunity Twenty cases of paralytic poliomyelitis had already been reported in 1959, when our study began during the second week of August Rectal swabbings from 1,892 persons—children

Table 1 —*Proportion of Children of Indicated Age Fed Single Dose of Trivalent Vaccine in Toluca, Mexico, August, 1959*

Age Yr	Persons of Indicated Age, No	Fed Vaccine No	Persons of Indicated Age Vaccinated, %
<1	3 195	2 965	90
1	2 803	2 327	82
2	3 257	2 361	71
3	3 329	2 453	74
4	3 298	2 575	78
5	2 886	2,410	83
6 10	11 708	10 942	93
<1 10	30 476	26,033	86
Total population all ages	103 072	26,033	25

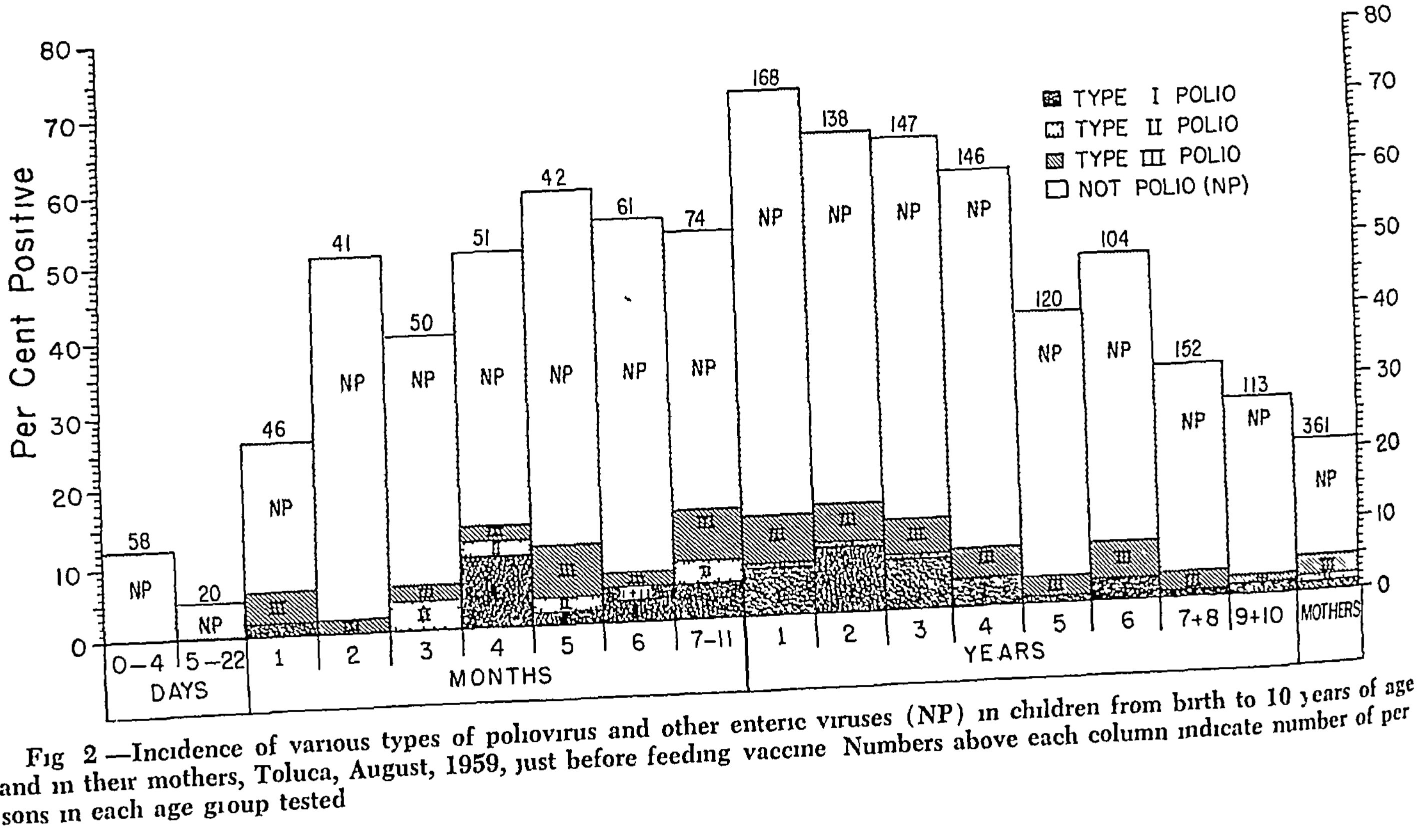


Fig 2 —Incidence of various types of poliovirus and other enteric viruses (NP) in children from birth to 10 years of age and in their mothers, Toluca, August, 1959, just before feeding vaccine Numbers above each column indicate number of persons in each age group tested

aged from birth to 10 years and their mothers—obtained at random in different parts of the city within a few days before the vaccination program, were each tested in monkey kidney and human epithelioma (HEP 2) tissue cultures as well as in newborn mice The results, summarized in figure 2, indicate that the special methods used revealed a much higher incidence of natural enteric viral infection than has ever been demonstrated before—beginning during the first days after birth and reaching a peak of 72% during the 1st year of life Beginning with 1-month-old children, polioviruses were isolated from every age group tested, with a peak rate of 14 to 15% in children between 7 months and 2 years of age The high infection rate among the mothers of these young children was surprising—5% for polioviruses and 16% for other enteric viruses

TABLE 2 —*Self-Limited Character of Dissemination of Polioviruses After Rapid Mass Oral Administration of Trivalent Vaccine in a Tropical Community**

	Before Vaccine Aug 1959	3 Mo After Vaccine
Total no tested	719	417
Incidence of polioviruses (P)	11.0%	0.7%
Incidence of other enteric viruses (NP)	50.8%	50.6%
Ratio NP/P	4.6	72.3

*Carrier rate of polioviruses and other enteric viruses among 1- to 5-year old children selected at random before and 3 mo after single dose ($10^{5.2}$-$10^{5.6}$ TCD_{50}) of trivalent oral poliovirus vaccine (Sabin) fed within a few days to 86% of children (newborn to 10 years) in Toluca Mexico

Carrier rate is based on detection of virus in single rectal swabbing—actual carrier rate is somewhat higher

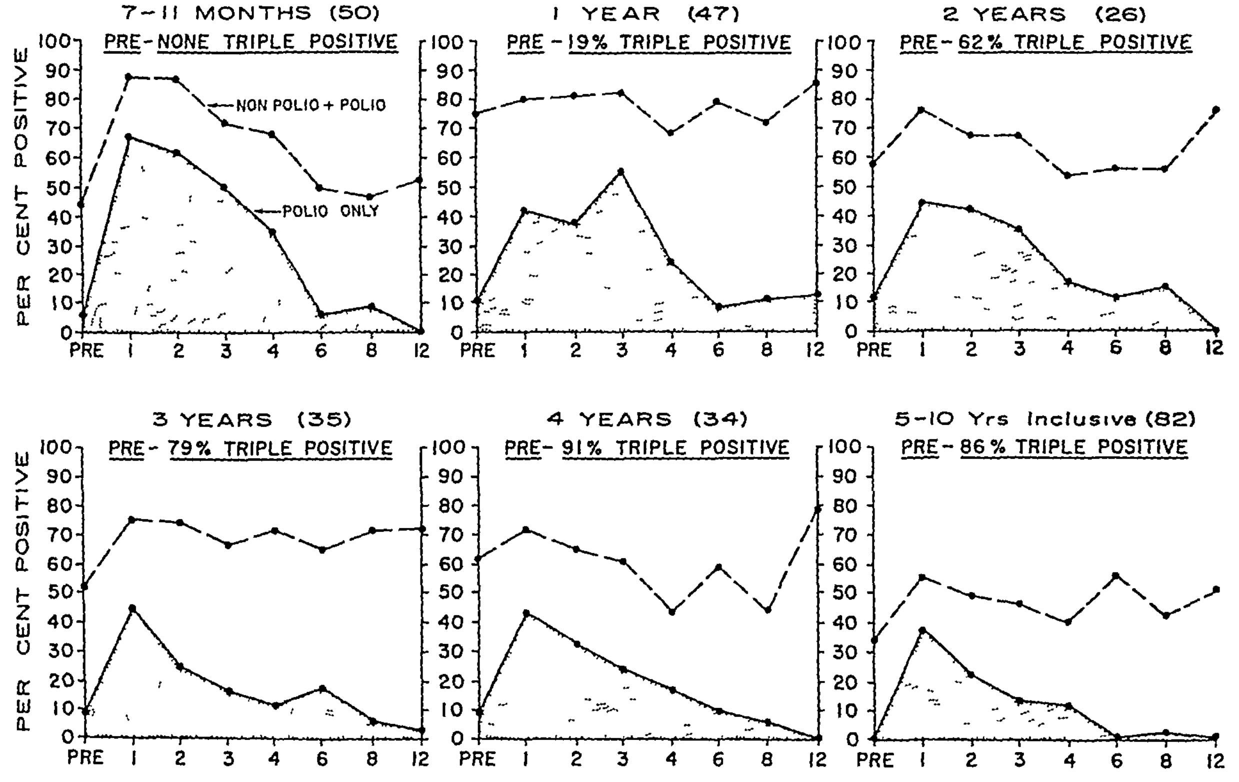


Fig 3 —Polioviruses and other enteric viruses in group of 274 children tested just before and at weekly intervals after single dose of trivalent orally given poliovirus vaccine, Toluca, August to November, 1959 Number in parenthesis next to each age group indicates number of persons tested

It was in this setting that a single dose of trivalent poliovirus vaccine ($10^{5.2}$ to $10^{5.6}$ 50% tissue-culture dose [TCD_{50}] of each type) was fed to a total of 26,033 children under 11 years of age—86% of all the children of this age group in Toluca The actual proportion of children of each age group who received the vaccine is shown in table 1 Only four days were required to feed the vaccine to 97% of the children who received it

To determine how effectively the attenuated polioviruses competed with the other enteric viruses and how long and extensively polioviruses continue to disseminate in such a community after this rapid and massive artificial seeding over 3,139 rectal swabbings were obtained during the subsequent three months and tested for virus A total of 2,711 viruses were recovered from the 5,031 prevaccination and postvaccination specimens, and the use of special methods permitted us to classify them rapidly as polioviruses or nonpolioviruses

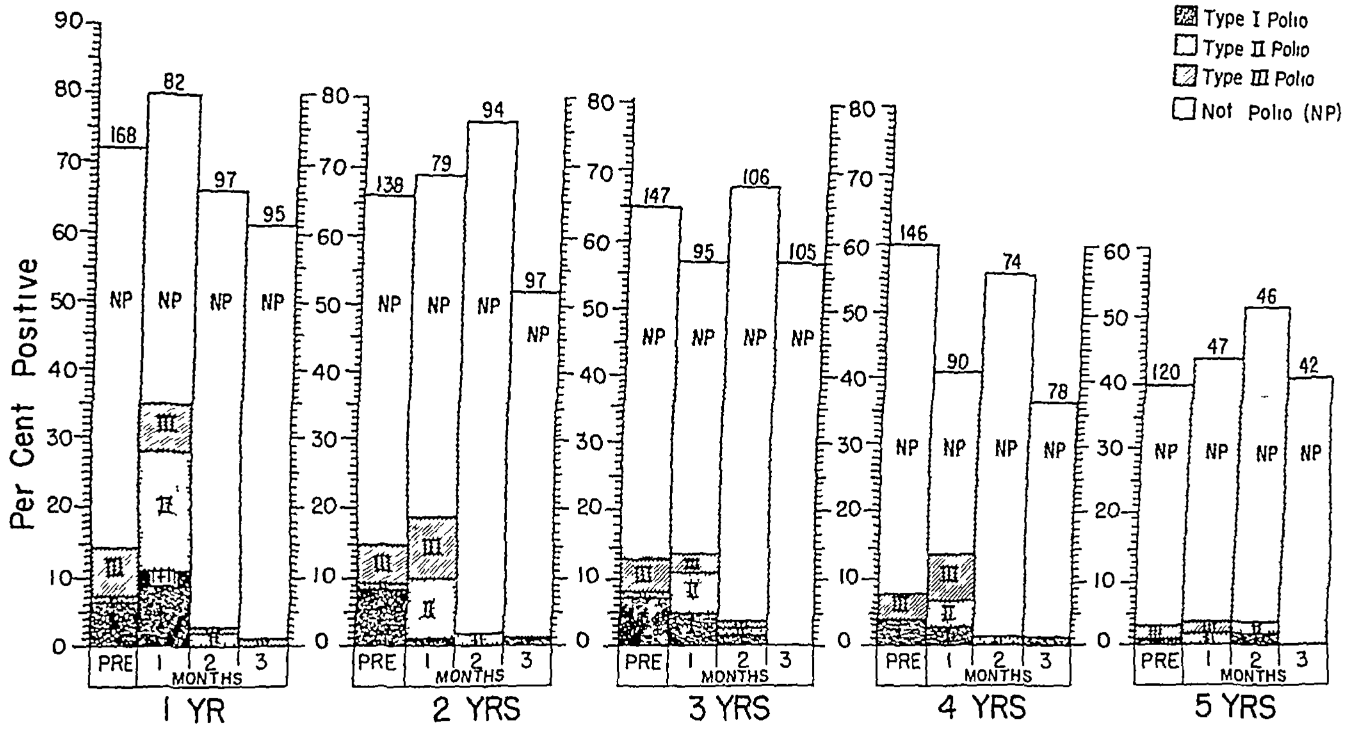
The results, shown in figure 3 for a group of 274 children who were tested repeatedly over a period of 3 months and in figure 4 for hundreds of different children randomly chosen before and at monthly intervals after vaccination indicate the following conclusions 1 While the total incidence of enteric viruses varied little or not at all during the three months, the polioviruses became dominant during the first three weeks after vaccination, the isolation rates being as high as 40 to 70% in the different age groups 2 The early dominance of the polioviruses was followed by a quick decline—more rapid in the children over 2 years of age—which by the end of three months reached a point that was markedly lower than before the mass feeding of the live polioviruses vaccine

TABLE 3—*Development of Poliovirus Neutralizing Antibodies During Comparable Ten-Week Period in Two Mexican Cities**

Type	Toluca—After 1 Dose of Trivalent Vaccine		Queretaro—No Vaccine	
	No †	%	No	%
1	36/53	68	2/33	6
2	63/77	82	3/31	10
3	33/76	43	5/38	13

* Conversion rates for indicated type are based on simultaneous tests on paired serums from originally negative children

† Children without antibody who were carriers of poliovirus at time first blood specimen was obtained are excluded from this calculation



Antibody % Positive	I	57%	83%	75%	96%	94%	97%	97%	100%	91 %	100%
	II	30%	83%	79%	100%	85%	97%	100%	100%	87 %	100%
	III	43%	77%	79%	88%	88%	91%	94%	100%	96%	96%

Fig 4 —Incidence of various types of poliovirus and other enteric viruses (NP) in 1 to 5 year old children randomly selected just before and at indicated monthly intervals after single dose of trivalent orally given poliovirus vaccine, Toluca, August to November, 1959 Numbers above each column refer to number of children tested during each period

The self-limited character of dissemination of polioviruses after this rapid mass feeding of live polioviruses vaccine, under conditions which favor the continued extensive dissemination of enteric agents, is strikingly brought out in table 2, which shows the results of tests on 1,135 randomly selected 1-to-5-year-old children The isolation rate of non-poliomyelitis enteric viruses was about 51% before and also three months after the vaccination program, while the isolation of polioviruses dropped from 11 to 0 7%, a sixteenfold diminution

The serologic effect of this temporary dominance of the polioviruses is shown in table 3, in which the antibody conversion rates during the first 10 weeks after the mass feeding of a single dose of trivalent vaccine in Toluca is compared with the natural antibody conversion rates in the city of Queretaro, which is similar in size, climate, hygienic conditions, and geography, but in which no vaccine was given The incidence of antibody conversion 10 weeks after the single dose of trivalent vaccine in single-negative, double-negative, and triple-negative children is shown in table 4 The extent of interference resulting from the simultaneous administration of all three types and the dominance of the type 2 strain in this mixture are clearly evident Thus, for type 1, the conversion rate was 100% in the small number of single-negative, 88% in the double-negative, and 55% in the triple-negative reactors, for type 3 it was 59, 42, and 37%, respectively, while for type 2 there was no difference in the three categories, the conversion rates being 82, 80, and 83%

An analysis of the data (table 5) on the children from whom rectal swabbings were obtained at weekly intervals indicated two significant facts 1 Many children who developed antibody did not excrete sufficient virus to be detected in the rectal swabs 2 Some of the children who had no demonstrable antibody at 10 weeks excreted enough poliovirus to be detected in at least one of the rectal swabbings obtained during the first 4 weeks When the children in the second category are included one obtains an estimated total infection rate of 80% for type 1, 87% for type 2, and 47% for type 3 during the first 10 weeks after the single trivalent dose of vaccine Further analysis of these data indicates that among the total number infected, antibody was demonstrable at 10 weeks in 86% for type 1, 94% for type 2, and 92% for type 3

The virological evidence of the marked drop in the dissemination of polioviruses that occurred 8 to 12 weeks after vaccination is supported by the serologic data shown in table 6, which indicate that among the children who failed to develop antibody during the first 10 weeks very few converted during the subsequent 11 weeks At this point the remaining negative children in the group that were being followed serologically were fed another dose of trivalent vaccine and they then exhibited a further marked immunogenic effect The total conversion rate after the two doses of vaccine was 96% for types 1 and 2 and 72% for type 3, despite the interfering effects resulting from the massive infection with other enteric viruses (which was still 55% in January, 1960) and the simultaneous administration of all three types of poliovirus The lower final conversion rate for type 3 may also be related to the fact that we did not use the pH test for low-avidity antibody, which occurs more commonly after infection with the type 3 virus It should also be noted that the second feeding was not a mass feeding but involved only 44 children under 4 years of age who were distributed among a large number of families throughout the city The results might have been even better if nature had been given another chance at dissemination of the polioviruses in the community by feeding all the children under 4 years of age another dose of the vaccine Figure 5

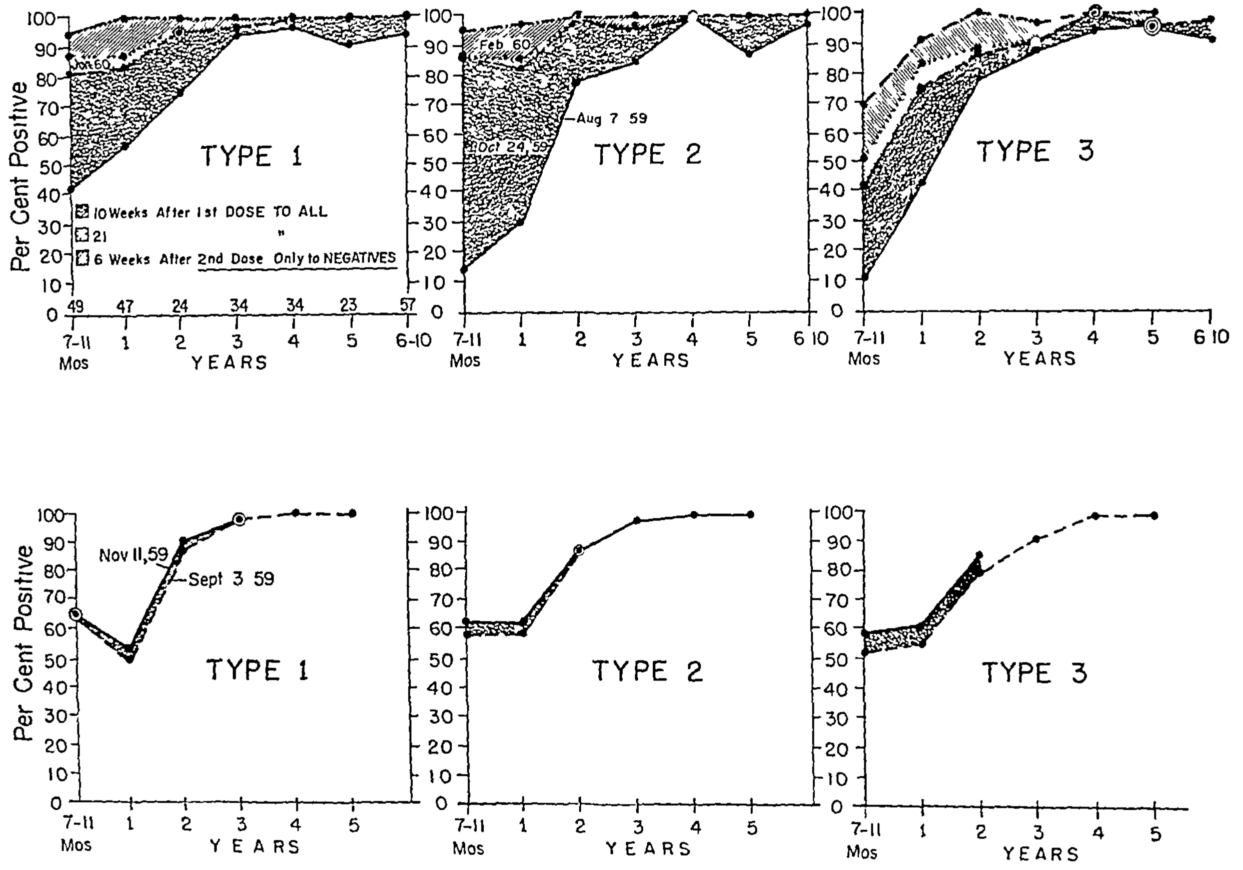


Fig 5 —Status of poliovirus antibody in two Mexican cities *top*, Toluca—vaccine given, *bottom*, Queretaro—no vaccine given Numbers above age groups in left upper diagram indicate number of children tested

TABLE 4 —*Poliovirus Antibody Conversion Rates in Toluca Among Single-Negative,' Double-Negative and Triple Negative Children Ten Weeks After Feeding Single Dose of Trivalent Vaccine*

	Single Negative		Double Negative		Triple Negative		Total	
Type	No Tested	% Converted	No Tested	% Converted	No Tested	% Converted	No Tested	% Converted
1	4	100	16	88	33	[illegible]	53	[illegible]
2	17	82	[illegible]	80	[illegible]	83	77	82
3	[illegible]	9	24	42	[illegible]	37	[illegible]	43

shows that with these two feedings of vaccine it was possible to achieve an immunogenic effect within a few months and without any cost in paralysis, comparable to that achieved naturally only after four years and at a price of about 56 cases of paralytic poliomyelitis

The comparable serologic effectiveness of the same lots and doses of vaccine used in trivalent or monovalent form under different conditions in children in northern climates is shown in table 7 It is evident that when the interval between the separate, sequential feedings of the three types was not less than four weeks, the antibody conversion rates were 100% or close to it, while the mixture of all three types yielded conversion rates of only 82, 80 and 71%, respectively, for the three types in a mixed group of single-negative, double-negative, and triple-negative children living under conditions that were conducive to natural spread of the vaccine strains among them These results, as well as other data collected by Russian investigators in 1959, indicate that the separate sequential administration of the three types of vaccine at intervals of not less than four to six weeks is optimum during the cold or cool months of the year in areas with good sanitation and hygiene

TABLE 5 —*Incidence of Virus Recovery from Rectal Swabs in Relation to Development of Antibody—Estimate of Total Infection Rate During Ten-Week Period After Single Oral Dose of Trivalent Vaccine in Toluca*

Category	Type 1		Type 2		Type 3	
	No	%	No	%	No	%
Virus in Rectal Swabs Among Those Who						
Developed antibody	12/36	33	52/63	82	21/33	64
Failed to develop antibody	2/17	12	3/14	21	2/43	5
Estimate of total infection rate	42/53	80	67/77	87	36/76	47
Development of antibody among total no infected (demonstrated + estimated)	36/42	86	63/67	94	33/36	92

TABLE 6 —*Conversion Rates at Different Times After Feeding Two Doses of Trivalent Poliovirus Vaccine in Toluca*

		% Converted at Indicated Time After			
		First Dose Mass Feeding		Second Dose Negative Only	
Type	Children Tested No	First 10 Wk Aug 1959 Oct 1959	Next 11 Wk Oct 1959 Jan, 1960	6 Wk Jan 1960 Feb 1960	Both Doses Aug 1959 Feb 1960
1	53	68	7	85	96
2	77	82	0	73	96
3	76	13	3	48	72

Conclusions

The results obtained in Toluca, Mexico, are of significance for the vast majority of the world population, among whom immunity to poliomyelitis is naturally acquired during the first few years of life at a varying and sometimes considerable price in paralysis In such areas the feeding of trivalent vaccine on two brief occasions at an interval of six to eight weeks to all children aged under 4 or 5 years, depending on the age incidence of recorded cases of paralytic poliomyelitis or on the result of a serologic survey in the region, constitutes a rational initial approach to the eradication of poliomyelitis The rapid disappearance of polioviruses from Toluca under the conditions of the present study indicates that the oncoming generations of children will have to be similarly vaccinated at the optimum time during the first 6 months of life, because they will have little or no opportunity for natural acquisition of immunity to poliomyelitis

This study was aided by a grant from the National Foundation

Elland and Bethesda Avenues (29) (Dr Sabin)

TABLE 7 —*Effectiveness of Aliquots of Same Lots and Same Doses of Vaccine Used in Toluca When Given to Children of Comparable Age During Winter and Spring Months in Northern Climates, Trivalent Versus Monovalent (1-3-2)*

Investigator Place Age of Children and Time of Year	Method of Administration	No of Children Without Antibody for Indicated Type	% Developed Antibody for Indicated Type		
			1	2	3
Smorodintsev Leningrad *U S S R* children's homes up to 7 yr May 1958	Trivalent *tested 4 mo* later all together in camp during summer	29 negative for 1 *54 negative for 2* 38 negative for 3	82	80	71
Smorodintsev, Leningrad children's homes up to 3 yr Feb March April 1958	Monovalent 4 wk interval tested one month after each type	147 negative for 1 65 negative for 2 67 negative for 3	97	100	96
Verlinde Leyden Holland individual families up to 14 yr May or Dec, 1957	Monovalent 3 wk interval	20 negative for 1 *18 negative for 2* 28 negative for 3	100	90	100

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CIRCULATION OF THE BRAIN

DIFFERENTIAL DIAGNOSIS AND TREATMENT OF CEREBROVASCULAR DISORDERS

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Recently developed diagnostic, therapeutic, and investigative techniques are opening up new and encouraging vistas for effective management of cerebrovascular accidents of various kinds The diagnosis of stroke is not sufficient, it is necessary to determine the vessel involved and the cause of its involvement Early cerebral angiography is urged as essential for the recognition of structural anomalies, functional derangements, or pathological changes Medical treatment must take into account the possibility of blood dyscrasias, disturbance of the clotting mechanism, and cardiovascular disease Surgical treatment is available for the correction of malformations, occlusions, and aneurysms

Interest in the cerebral circulation appears to be greater today than at any time since Hippocrates first described apoplexy[1] Because cerebrovascular accidents are among the most common causes of death and disability in this country,[2] they have become the subject of intensive diagnostic, therapeutic, and investigative endeavor Therefore, the current methods of diagnosis and medical and surgical therapy will be discussed after certain aspects of the cerebral circulation have been considered

Cerebral Circulation

Anatomically, the cerebral arteries have a comparatively thin muscle layer and weak adventitia that render them unusually susceptible to rupture as the result of disease[2] Like all other vessels, however, they are endowed with both sensory and motor nerve fibers

The circle of Willis[3] and supratentorial venous channels[2] derive their sensory innervation largely from the first division of the trigeminal nerve Pain arising from a supratentorial vessel, as from an aneurysm, may therefore be experienced as ipsilateral orbital or temporal pain that may even resemble migraine On the other hand, pain from a posterior fossa vessel is referred via the vagus nerve and upper cervical roots to the suboccipital area or ear

Motor innervation of the cerebral arteries, mainly vasoconstrictor in nature, is ordinarily weak, although acute vascular trauma may induce marked vasoconstriction[4] The motor innervation of the carotid tree is mainly derived from the superior cervical sympathetic rather than the stellate ganglion,[5] which may be one reason why stellate blocks are so often ineffective in the treatment of patients with suspected or proved cases of cerebral vasospasm Sympathetic blocks are, of course, useless if infarction has already occurred

The vertebral-basilar system has a similar sympathetic nerve supply and connections from the 9th, 10th, and 12th cranial nerves[4] The facial nerve is said to supply vasodilator fibers to the cerebral arteries[6]

Cerebral arteries respond to local metabolic needs and increased blood carbon dioxide levels by dilatation They resemble the coronary arteries in remaining open when peripheral vessels constrict as a result of shock Like other vessels, however, they respond to mechanical or chemical irritation by local constriction or spasm[4] The local cerebral vasospasm that follows rupture of an intracranial aneurysm[7] may be explained by such mechanisms

Arterial muscle contraction secondary to local vascular insult is apparently more potent than neurogenic factors in the cause and spread of cerebral vasospasm Serotonin, a powerful vasoconstrictor, released from platelets of extravasated blood may be another factor that initiates or perpetrates vasospasm, according to recent studies[8] Clinically such vasospasm, often lasting two to three weeks, may become so widespread as to cause edema, ischemic softening, or infarction of the brain[9]

While vasoconstriction is probably not significant in most cerebrovascular accidents, it may be in some It certainly seems to play a role in some cases of migraine, essential hypertension, retinal angiospasm, and toxemias of pregnancy This is suggested by the intermittent character of symptoms and the segmental fusiform constrictions of retinal arteries that come and go as one watches the optic fundi in some of these cases

Collateral circulation in the brain can be just as effective as elsewhere[4] That it can begin immediately after local vascular occlusion has been shown during intracranial aneurysm surgery[10] When an aneurysm is opened after temporarily shutting off its main blood supply inside the head with special clips, there is always some arterial backflow mediated by adjacent cerebral arteries Such observations explain why cerebral arteries may at times become pathologically occluded without appreciable clinical signs Collateral circulation can develop between terminal branches of all of the major cerebral vessels[11] It may also develop from branches of the external carotid artery through ophthalmic,[12] middle meningeal, and other connections[2]

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Cerebral infarction softening, or edema occurs when an adequate collateral circulation fails to develop Factors contributing to such failure include systemic hypotension, existing arterial disease, an increased blood viscosity, clotting, or sludging tendency, polycythemia[14], aggregation of red blood cells induced by a fatty meal[14], dehydration by substances of high molecular weight such as dextran or polyvinyl pyrrolidone (PVP)[15], anemia, leukemia[16], severe cerebral vasospasm, or congenital anomalies of the circle of Willis Of the latter the most common is maldevelopment of an anterior cerebral or posterior communicating artery If either of these key links in the circle of Willis is defective, as it is in at least 25% of all persons with aneurysms,[16] the development of an adequate collateral circulation may be precluded

Finally it should be noted that cerebral veins as well as arteries are subject to thrombosis[17] that may also give rise to symptoms and signs resembling those of a stroke

Incidence

A so-called stroke may be due to either an occlusive or a hemorrhagic process Vascular occlusion, usually arteriosclerotic or thrombotic, is the cause of about 65% of all strokes[2] Intracranial arteries are affected in about two-thirds and arteries of the neck or upper part of the thorax in one-third of these cases The fact that partial occlusion is somewhat more prevalent than total occlusion of extracranial vessels[18] lends hope for greater therapeutic success Hemorrhage of various kinds accounts for 20% of strokes and emboli for 5%[2]

In 600 cases of strokes recently reported by Gurdjian and others[18] the onset, though apoplectic in 36% of the patients, was slowly progressive in 18% and characterized by recurrent symptoms or signs in 46% These data also suggest that many of these patients could be helped if given the benefit of more timely diagnosis and treatment

Diagnosis

Accurate clinical diagnosis depends on the history, the physical and neurological examinations, and various special tests Inspection of the optic fundi and, if possible, evaluation of the visual fields are important Carotid artery occlusion in the neck may be suggested by reduction of ipsilateral retinal artery pressure,[19] poor or absent carotid pulsation in the neck and pharynx,[19b] and a contralateral cranial bruit[20] It should be emphasized that a history of episodic symptoms such as intermittent numbness, as pointed out by Hippocrates,[1] or paresis may indicate an incipient stroke and the need for prompt diagnostic studies, including angiography

Ancillary tests include appropriate blood studies, roentgenograms of the skull and chest, electrocardiography, electroencephalography, and lumbar puncture for cerebrospinal fluid (CSF) studies, including a blood cell count Cerebral angiography,[21] the most valuable test of all, is relatively safe, with only a 2% incidence of complications, occurring usually in very ill patients Angiography can usually reveal what type of disease exists, what arteries are affected, and more specifically, in the case of occlusive disease, whether extracranial or intracranial arteries are involved or whether intracranial hemorrhage is due to a ruptured aneurysm

Treatment

Treatment is either medical or surgical depending on the location and nature of the lesion About one-third of patients with occlusive disease of cerebral arteries or veins may be benefited by anticoagulation therapy This therapy is contraindicated by fresh hemorrhage, a recent infarct, or high blood pressure[22] Infarction may sometimes be indicated or followed by special CSF enzyme studies[23] Fibrinolysins have so far proved of value only if given early[24] Cardiac arrhythmias, a common cause of emboli, and polycythemia, leukemia, and an increased clotting tendency should be corrected by appropriate drug therapy

Carotid Occlusion—For properly selected cases of carotid artery occlusion in the neck, surgical intervention has much to offer Patients who respond best are those with partial unilateral occlusion who have suffered from intermittent or progressive symptoms[25] These symptoms are often precipitated by postural hypotension, as indicated by the history and sometimes by appropriate tests, including electroencephalographic changes on a tilt table[26] Endarterectomy, first done by Dos Santos in 1949,[2] is most frequently required at the origin of one internal carotid artery and should be done promptly before complete occlusion and hemiplegia occur There is little risk of any sort from this type of surgery

Patients with complete occlusion of long standing cannot be helped because of permanent brain damage and should not be operated on if effective collateral circulation has already developed When, however, acute occlusion is treated by emergency angiography and endarterectomy within three or four hours,[27] the collateral circulation of the brain is sometimes adequate, so that some of these patients are improved

Intracranial endarterectomy of vessels such as the middle cerebral artery has not proved successful, although earlier angiography and improvements in small vessel surgery[28] give hope for the future in this domain

Vertebral artery insufficiency may also be indicated by postural hypotension that gives rise to dizziness, sudden weakness of the legs, oculomotor symptoms, and perhaps other symptoms such as ataxia Such insufficiency may be due to occlusive disease,[18] compression,[29] or polycythemia,[17b] each of which can often be alleviated by appropriate surgical or medical therapy

The syndrome of syncope from a hypersensitive carotid sinus reflex,[30] while rare, should be considered in the differential diagnosis as well as other conditions such as brain tumor,[31] carotid thrombosis due to trauma,[32] or a cervical rib[33]

Hematoma—Surgery is indicated for prompt evacuation of massive intracerebral hematomas, which are usually secondary to vascular hypertension but are sometimes caused by bleeding from a small angioma,[34] arteriovenous malformation, brain tumor, or intracranial aneurysm Without surgery the mortality is 98%, with surgery it is 28%[35] Cerebellar hematomas[36] are rare and are apt to cause marked respiratory depression as well as lethargy and coma

Arteriovenous Malformations — Arteriovenous malformations[37] are congenital anomalies composed of serpentine arteries and veins that extend into the brain in a wedge-shaped manner About 50% give rise to intracranial hemorrhage Since they tend to enlarge with age and frequently give rise to convulsive seizures or other symptoms as they destroy the brain or interfere with its circulation, their surgical removal is advisable whenever feasible Treatment by artificial emboli has been reported[37b]

Aneurysms—In over 50% of all patients with cases of subarachnoid hemorrhage treated at the Neurological Institute, bleeding has been due to rupture of an intracranial aneurysm[38] It is important to note that these lesions, first described by Morgagni in 1761,[7] may be associated with arteriosclerosis or long-standing vascular hypertension in one-third of such patients Since these two diseases could easily lead to an erroneous diagnosis of a stroke, prompt angiography is recommended whenever an aneurysm could be the cause of subarachnoid hemorrhage

After rupture of an intracranial aneurysm the mortality without surgical treatment is over 50%[39] Carotid artery ligation in the neck often proves ineffective, especially for anterior[8] or middle cerebral artery aneurysms, and has led to a high mortality and an 18% incidence of hemiplegia or other complications[40] By far the best treatment, if the condition of the patient is reasonably good, is direct intracranial surgery This approach is often imperative because of anomalies in the circle of Willis that would prevent adequate collateral circulation if a carotid artery were clamped or ligated in the neck

Present procedure involves prompt bilateral angiography followed by craniotomy under hypothermia when the patient's temperature is 28 C (82 F)[39] The hypothermia protects the brain when blood flow is reduced by clips temporarily placed on key branches of the circle of Willis to reduce pressure within the aneurysm and prevent it from bursting Thanks to studies in the laboratory and operating rooms on the effects of hypothermia and central stimuli on cardiac action,[41] there have been few cardiac complications such as serious arrhythmias The use of intravenously given urea,[42] a powerful diuretic, has also aided cranial surgery by reducing brain volume and thus making the exposure easier

With cranial surgery of ruptured aneurysms as now practiced, the operative mortality has been reduced from over 30% to 15% and for some types of aneurysms to 7%[10]

Summary

All patients with stroke should have prompt and adequate examination, including greater use of early angiography, as an aid to medical or surgical therapy The diagnosis of stroke should be avoided in favor of a more specific designation, such as occlusion of a given artery or hemorrhage from a given cause Again, early cerebral angiography is urged for this purpose

Aspects of the cerebral circulation, including innervation, vasospasm, collaterals, and anomalies, are frequently important in the diagnosis and management of various cerebrovascular lesions Medical treatment requires careful attention to the local lesion by anticoagulation or fibrinolysin therapy, when indicated, and treatment of blood dyscrasias and the systemic circulation as a whole, including the maintenance of an edequate blood pressure and cardiac action It is emphasized that surgical intervention is of value for the treatment of partial occlusion of arteries in the neck, for evacuation of massive intracerebral clots, and for intracranial vascular malformations and ruptured aneurysms

In conclusion, it can be said that recently developed diagnostic, therapeutic, and investigative techniques are opening up new and encouraging vistas for more effective management of cerebrovascular accidents of various kinds

NOTE All references cited will be available in the reprints

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COMPULSORY HEALTH INSURANCE—The first application of such ideas was made possible by the concomitant development of the principles of insurance English towns, providing local medical relief under the Poor Law system, resented expenses thrust on them by transient laborers Parliament was therefore persuaded during the 1750s to require that coal heavers on the Thames make prepayments to a fund which would meet their costs in case of illness With this example in view, reformers urged by the late 1700s that compulsory health insurance should be required of all workers throughout the country Similar ideas were advocated in the Revolutionary assemblies at Paris during the 1790s and apparently would have been applied had it not been for military emergencies—R H Shryock Medicine and Society in America 1660 1860 New York University Press 1960 page 106

HOME CARE OF CANCER PATIENTS

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A program of home care was organized in 1950 to provide the services of physician, nurse, and social worker for cancer patients who did not require hospitalization yet were too ill for treatment at the clinic. Under the direction of a physician, the program coordinated the resources of hospital, clinic, medical school, and community. This team concept has benefited all participating groups. In nine years of operation this program has achieved a plateau, with a patient load of 15 to 25 patients and about 4,500 patient-days of care per year. It demonstrates that care in the home, when practical, is less expensive and more conducive to the patient's general well-being than is hospital care.

The cancer home care program of the George Washington University was organized when the Alexander and Margaret Stewart Trust Fund offered a grant to establish such a program in January, 1950.[1]

Many factors had changed the pattern of medical care over the previous half century and created the need for a program for the care of cancer patients at home. Earlier attitudes of hospital benevolence for the chronically ill and/or the indigent patient had changed, mainly due to increasing hospital costs, business-type management, and decreased endowment.[2] Patients who had a long-term illness and long-term convalescence were being sent home or to nursing homes.[3] For the nonindigent, physician care in his home was usually adequate, but for the indigent patient who was confined to his home and did not require hospitalization, there was no available medical care. The home care program was an answer to this problem.

The home care program of the George Washington University Cancer Clinic was patterned after the successful one at Montefiore Hospital, New York City; the primary aim was to provide, in a patient's own or nursing home, medical, nursing, and social service care of the highest obtainable quality to cancer patients who are too ill to attend the clinic but do not require continuous hospital care.

The program was established as a part of the George Washington University Cancer Clinic.[1] The patients are referred to the program from clinics, hospitals, and other sources in the community. Complete laboratory, diagnostic, and therapeutic roentgenographic facilities of the clinic and hospital are used. Clinical, therapeutic, or diagnostic procedures, whenever possible, are performed at the patient's home by use of special instrument packs provided by the Clinic. Sometimes a patient is brought to the clinic or hospital for a procedure such as roentgenography. Not only does the home care program freely use the services of the hospital and clinic, but these latter facilities also use the services of the home care program to attend acutely ill patients at home and for follow-up care of the postsurgical patients.

Home care is not designed as a replacement for hospitalization or outpatient care but to complete the triad of necessary facilities required in the care of chronically ill patients. The service is based on team concepts[1] utilizing the services of doctor, nurse, and social worker. Each works with the others in the care of these patients at home. Team concept is essential.

Personnel

Physician Care.—The director of home care is a physician, trained in internal medicine with special reference to cancer. However, consultation with surgical, and auxiliary medical and research personnel is readily available as all patients are discussed at routine home care conferences by the home care team and are presented as needed to the weekly tumor conference. The director, also, is responsible for the use of the program facilities in teaching how to care for patients with cancer to medical students as part of the medical school training.

Visiting Physicians.—Visiting physicians are responsible for the daily care of assigned patients and make routine visits to the patients at home, the frequency is determined by the needs of the patients. They collect specimens as necessary, bring them back to the laboratory for study, and perform necessary home procedures such as thoracentesis, catheterizations, and intubations. They call the other members of the home care team if the need arises. The visiting physician reports the patient's condition and special problems in his reports of each visit and at the home care conference, so that members of the team are always aware of the patient's current status. Problems of special patients are summarized and presented by those physicians to the weekly hospital tumor board together with pertinent social service evaluation for determination of long-term patient care.

Immediate treatment is largely decided by the visiting physician, although this is discussed and may be modified in the other conferences. Decisions regarding long-term care are made after consulta-

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tion either with a specialist, the research physician concerned with the problem, or the tumor board The visiting physicians also rotate for emergency night calls They may also see and care for clinic cases at home who are not on home care, if an emergency arises All visits and findings are noted and recorded on the patient's chart by secretarial service to maintain a complete clinical record

The patients are assigned to visiting physicians on a geographical basis to keep the house calls as convenient as possible As has been true with the New York City and other home care programs, it has been difficult to obtain young practicing physicians with enough time in their schedules to permit this type of service Thus, there is frequent change in the visiting medical personnel

Nursing Care—Nursing care, which is provided by the Visiting Nurse Association,[5] the Public Health Nurses of the District of Columbia, and surrounding communities, is under the direction of the visiting physicians Such care consists of routine bed care, dressings, intubation, colostomy care, and other nursing procedures as ordered by the visiting physician Nursing observations are recorded Families are instructed in various types of care that they can provide Reports of the patient's condition are routinely relayed to the physicians Excellent cooperation, coordination, and integration has been achieved in this field

Social Service—Social service facilities are essential as home care for cancer patients always involves a seriously and chronically ill patient surrounded and attended by an emotionally involved family Interfamily stresses and varied patterns of behavior by the patient and toward the patient require a social worker with good judgment The social service workers must calm the fears before they are recognized, must establish the family's realization of the patient's extreme illness, and yet must help all to control their emotions so that each may work to the patient's benefit The social worker must keep the patient and family content in the fact of pain and other environmental circumstances which would disturb anyone

In our program the social service worker performs other tasks such as arranging for housing, prescribed equipment and ordered medicaments and arranging for the patient's transportation and the use of other community resources as needed In short, all applications, arrangements, and plans for home care are channelled through the social service department

Other Members—Other workers are used as needed for the patient's benefit Occupational therapists are used for diversion and occasionally for therapeutic or self-employment possibilities The Heart Association and Good Will Industries have cooperated Physical therapists are at times essential, particularly for a patient with neurological or orthopedic problems, who has been given braces The American Cancer Society provides dressings and also underwrites some additional nursing service Several organizations have provided additional transportation for patients, medicaments, and equipment These community resources may be considered as part of home care

Because of the unique affiliation with a teaching-research clinic and hospital, new and even experimental drugs are used in an attempt to help the patient Sometimes, the treatments are started in the hospital or clinic, and because of uninterrupted continuity of care between home care, hospitalization, and clinic, are continued without change while the patient is on home care

Teaching

In addition to the service aspect of the home care program, its facilities are used as a teaching service for medical students at George Washington University Each week a patient is selected who presents a problem or interesting findings, and students are taken in groups of two or three to the patient's home En route, through prior study of the patient's chart, the case is presented to the instructor by the students in the same manner as a case being presented to a conference The ability to do a thorough examination under home conditions is stressed, and its need is emphasized Findings are reviewed with the instructor and students during the return trip to the clinic, the patient's general status is discussed and methods of procedure reviewed This has provided a unique opportunity for teaching students in techniques of home medical visits, a field which was previously omitted in their course of study

New Phase of Student Teaching—Recently we have initiated a new phase of student teaching during which time students are assigned an individual patient for home visit, examination evaluation, and report This occurs during the time of the students' assignment to the cancer clinic Just prior to the end of each group of students service at the cancer clinic, a conference with the visiting physicians, students, and entire home care personnel is held and the student caring for an individual patient presents his case The entire conference then discusses the findings, evaluations, and suggestions for further care In this limited time the student participation by assignment to patients has been received enthusiastically and felt to be of tremendous teaching value

Discussing Problems with Patients—As far as is practical, our patients have the diagnosis disclosed and discussed with them[1] There are a few instances, when the family wishes that the patient not be informed or where, because of emotional instability, such disclosure is unwarranted The family is kept aware of the current medical status In every instance a strong, cheerful attitude is used as though always expecting improvement for the patient This positive approach adds hope and lessens despair[6] Our cases run the gamut from long-term incurably ill patients maintained at home to many more frequent short-term cases

Comment

Prerequisites for Successful Care—Prerequisites for successful care of a patient include (1) adequate home environment, (2) complete medical evaluations and work-up, (3) medical condition of the patient such that care can be administered at home, yet patient should not be so well that he can attend outpatient department, nor so ill as to require hospitalization, and (4) a home with adequate physical facilities, such as adequate bedroom space

Costs—In the nine years of operation of our program, the patient load has achieved a plateau of about 15 to 25 patients In terms of patient days of care, about 4,500 patient days of care are supplied per year Costs have not been accurately determined but the home care service of the New York City municipal plan was reported to cost approximately $10 38 per patient per day in 1949 and $21 66 for hospital care[7]

Monetary savings to the community have been stressed, and although this is a very considerable advantage, the advantages to the patients are much more important Prior to home care programs, most patients were confined to the hospital or similar facilities for many months Although measurable proof is hard to obtain it is felt that the patients exhibit greater contentment at home and maintain better physical health for a longer time Apparently such things as devotion, comforts of home, and catering to one's whims of diet do make for a decided difference in the patient's health and attitude At home he is still a member of the family, helping with family discussions and sharing neighborhood interests

The home care program has been successful in providing good medical care to a previously neglected group of patients and in teaching special patient care to which medical students had not previously been exposed

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SOLITARY COIN LESIONS OF THE LUNG

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and

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Pulmonary lesions described as coin lesions because of their roentgenographic appearance were studied in 95 patients The study was limited to solitary lesions, homogeneous or calcified, 1 0 to 4 5 cm in size, round or oval in shape, with sharp borders surrounded by normal lung, found during the examination of asymptomatic patients The final diagnosis was based on histological examination This showed the lesion to be malignant in 6 cases In 55 cases it was a fibrocaseous granuloma, and in 14 it was a tuberculoma The size of the lesion was not significant Calcification in a solitary pulmonary nodule is a good but not an absolute sign that it is benign The authors believe that solitary pulmonary lesions, with few exceptions, should be excised and examined histologically

The asymptomatic patient with a solitary pulmonary lesion which has been discovered on routine chest roentgenogram presents a difficult diagnostic problem Although the need for an accurate and specific diagnosis is usually appreciated, it is of the utmost importance to use the most direct diagnostic approach Many aids to differentiate benign from malignant processes have been described in large series of cases However, these are rarely specific enough in any one case to justify a significant delay in subsequent management This urgency in diagnosis is due to the significant percentage of early malignancy of lesions, active tuberculosis, and arteriovenous fistulas found in reported series

Review of Literature

Many articles concerning coin lesions of the lung, together with series of cases, have been published noting varying percentages of malignant lesions,

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From the U S Naval Hospital, St Albans, N Y Dr Pischnotte is currently at the U S Naval Hospital, Navy 115 Dr Sammons is currently at the U S Naval Hospital, Pensacola, Fla tuberculosis, and other diagnoses This is accounted for in part by the different criteria used by various authors to define the coin lesion Some case series are limited only to asymptomatic patients, others place restrictions on size or calcification of lesions Nevertheless, all authors agree that a significant number of such lesions are malignant, the incidence varying from 7 3%[1] to 70%[2] In a review of 1,423 cases, Mitchell and Taylor[3] found malignant lesions to represent 42% (3% of which were bronchial adenomas) of the total The possibility of malignant condition must therefore be uppermost in the mind of the physician when confronted by a patient with a coin lesion

Tuberculomas, since they harbor viable tubercle bacilli, are a definite threat to the health and life of the patient The lesion may break down and produce local cavitation, tuberculous pneumonia, endobronchial spread, or even miliary dissemination Although the mortality associated with these complications has been markedly reduced with present-day chemotherapy, the prolonged therapeutic regimen and subsequent morbidity argue strongly for a preventive attitude It is generally agreed that such lesions are best treated by surgical excision The reported incidence of tuberculomas varies from 4%[4] to 40%[5] Mitchell and Taylor[3] found that they represented 20% of the 1,423 cases reviewed Many reports have included all fibrocaseous granulomas as tuberculomas, and only recently has the actual demonstration of viable tubercle bacilli been widely recognized as a prerequisite for this diagnosis Many pulmonary granulomas have been shown to be due to Histoplasma capsulatum, with a reported incidence as high as 8%[5] Coccidioides immitis may also cause such lesions, particularly in endemic areas, it accounts for 18% of coin lesions in the report of Higginson and Hinshaw[6]

A third less common but potentially dangerous lesion is the arteriovenous fistula The patient who is fortunate enough to have such a lesion diagnosed in its asymptomatic stage usually requires only wedge resection of the involved area However, many of these patients do not present themselves for diagnosis until such severe complications as meningo-encephalitis, brain abscess, cerebrovascular accidents, and hemoptysis have occurred[7] Because 3 to 5% of solitary pulmonary lesions are arteriovenous fistulas,[5] the differential diagnosis must include this potentially serious entity

The remainder of pulmonary coin lesions consists of harmartomas, nonspecific granulomas, and other rare entities It is unfortunate that these generally innocuous lesions cannot be diagnosed with certainty by routine methods[8]

Diagnostic Procedures

Solitary pulmonary coin lesions are discovered on routine chest roentgenograms, and thus this study is of primary importance in diagnosis Roentgenologic studies will often show the presence of calcium in the lesion Tomography is often required to demonstrate smaller calcific deposits The demonstration of calcium in the lesion, especially if it is dense or laminated in a central nidus, is a strong argument for benignity of the lesion[9] However, several cases reporting calcification in malignant coin lesions have appeared,[10] and calcium can be demonstrated even more often in the surgical specimen[11] Thus calcification cannot be regarded as absolute assurance of the benign nature of the lesion

In some cases of malignancy of the lesion, tomograms may demonstrate local perivascular and peribronchial invasion Rigler[12] has described a notch sign' seen in some coin lesions which have been invariably malignant However, even if neither of these signs is apparent, the lesion may still be malignant

Although fluoroscopic examination can often document how sizes of pulmonary arteriovenous fistulas are changed by respiration, angiocardiographic examination is the study of choice This method definitely demonstrates the vascular nature of the lesion and is of the utmost importance in detecting multiple lesions[7] In cases of malignancy the angiocardiogram may show abnormalities of the pulmonary vasculature such as invasion, deviation, and abrupt termination of vessels[13]

Roentgenologic studies beyond those discussed previously only will delay definite diagnosis and rarely will aid in differentiating the various causes of coin lesions Nevertheless, a reasonable presumptive diagnosis can be reached in many cases by considering the foregoing together with such factors as age and sex of the patient and location and size of the lesion Thus, malignant lesions are more common in persons over 40 years of age and in men Tuberculomas are rare anteriorly and in the basilar segments Symptoms such as cough, hemoptysis, and sputum production greatly increase the chances of malignancy in a lesion or the presence of tuberculosis Coin lesions which are over 5 cm in diameter are malignant in the majority of cases But even with all these factors taken into account, only the arteriovenous fistula and occasionally malignant condition can be definitely diagnosed by roentgenologic studies and separated from all the possible causes of coin lesions In the majority of patients, therefore, roentgenologic studies are necessary and helpful but not definitive

Patients who show coin lesions usually undergo many other studies[14] Among these are skin tests in which positive results prove nothing of value and negative results only increase the chances of malignancy of the lesion Sputum examinations for acid-fast bacilli and malignant cells rarely show positive results, but when they do they are most helpful Similarly, bronchoscopy and examination of bronchoscopic washings rarely yield definitive information, chiefly because of the peripheral location of the lesions under consideration

After all these studies the physician and patient are generally faced with the problem of a solitary, circumscribed pulmonary lesion of questionable and potentially serious etiology In a follow-up study of patients discovered harboring coin lesions on a roentgenologic survey, a death rate of three times the statistically expected was found [15] Thoracotomy is therefore indicated as both a diagnostic and therapeutic measure and should be used without undue delay

Present Series

In 1953, Storey and others [1] reported 40 cases of coin lesions of the lung from this hospital all of which were proved by surgery and pathological examination These patients were mostly young, asymptomatic male patients who were on active military duty The criteria used to define the coin lesion were, (1) 1 to 5 cm in size, (2) round or oval with sharp borders, (3) surrounded by normal lung, (4) asymptomatic, (5) homogeneous or calcified, and (6) solitary

In the present series of 95 asymptomatic patients seen and diagnosed histologically since the previously mentioned report, the same criteria have been adopted with the exception of a limit on size of the lesion (actual range of size was from 1 to 4 5 cm) Completely calcified peripheral nodules are not included in this series There were 86 male patients and 9 female patients with an average age of 32 2 years and a median age of 32 years This distribution is a normal and expected one in a military hospital The various age groups were represented as follows 18 to 20 years of age, 5 patients, 21 to 29 years of age, 35 patients, 30 to 39 years of age, 33 patients, 40 to 49 years of age, 17 patients, 50 to 59 years of age, 4 patients, 50 years of age and over, 1 patient

The table lists the pathological diagnoses together with the average age, types of calcification if any, and responses to skin tests in these cases

The six cases of malignant lesions included three bronchogenic carcinomas in patients aged 32, 32, and 52 years, one bronchial adenoma in a patient aged 35, and one terminal bronchiolar carcinoma in a patient aged 48 A nodule, which developed in the single female patient in this group, was a metastatic deposit of malignant melanoma and was removed by wedge resection The primary lesion had apparently been removed from the patient's back some years previous without submission for pathological study

An evaluation of the distribution by site of the various types of lesions listed in the table yielded no significant information except that, of the 14 lesions proved to contain viable tubercle bacilli, 13 were in the apical-posterior segments of the upper lobes or in the superior segments of the lower lobes with 10 on the right and 3 on the left This distribution is similar to that of adult tuberculosis Of the fibrocaseous granulomas, in which neither acid-fast bacilli nor fungi could be demonstrated, only 35 (64%) were located in similar sites, 21 on the right and 14 on the left

Pathological Diagnoses, Age, Calcification, and Skin Test Response in Ninety-five Asymptomatic Patients with Coin Lesion

Diagnosis	Patients No	% of Total	Female Patients	Average Age (Yrs)	Calcification						Skin Tests†							
					No	%	Central	Flecks	Laminated	Ring	Pos	Unk	P	H	P & H	H & C	All Pos	None Pos
	95	100	9	32 2	41	43	20	19	1	1	63	14	24	17	19	2	1	18
Malignant	6	6	1	40 [illegible]							4		3	1				2
Benign	89	94*	8	32 0	41	47	20	19	1	1	59	14	21	16	19	2	1	16
Fibrocaseous granuloma	55	58	5	24 1	27	49	15	10	1	1	38	8	9	12	15	1	1	9
Tuberculoma	14	15	1	31 0	7	50	2	5			11	3	10		1			
Hamartoma	6	6	1	21 8	3	50	2	1			2		2					4
Histoplasmoma	5	5		33 0	1	20	1				5			3	2			
Arteriovenous fistula	3	3		21 3	1	33		1										3
Coccidioidoma	2	2	1	23 5	2	100		2			1	1				1		
Fibrocaseous granuloma with cavitation	2	2		32 0							1	1			1			
Organized pneumonia	1	1		20 0								1						
Fibrous nodule	1	1		52 0							1			1				

* Individual percentages of total add up to only 93% due to rounding off of numbers
† Pos Positive, Unk Unknown P PPD H Histoplasmin C coccidioidin

Analysis of the lesions in this series in regard to size yielded no significant information

Comment

A review of the above data is of interest in several respects As emphasized in the literature, calcification in a solitary pulmonary nodule is a good but not an absolute sign of benign condition None of our six malignant cases revealed any calcification within the lesion Also, the tendency for malignancy to occur generally in the older age groups is supported by this study although two cases occurred in persons who were 32 years of age If all of the patients less than 30 years of age in this series are excluded the incidence of malignancy increases from 6% to 11% This, however, is still a low percentage when compared to many reports in the literature, but it is a result of the patient population available to a military hospital

The location of tuberculomas in areas most susceptible to acid-fast bacillus infection is noteworthy as is the almost 100% presence of positive reactions to PPD tests in this group The fact that calcification was present in one-half of these cases demonstrates that, although this finding may be a good sign of the nonmalignant nature of the lesion, it does not prove it to be harmless The positive reactions given to skin tests by patients with the fibrocaseous granulomas may point to an etiological agent, but since no organisms were demonstrable in these this would be merely conjecture Only five patients with definite histoplasmosis and two with coccidioidomycosis were observed, but increasing use of cultures and such special stains for fungi as the periodic acid Schiff, should increase this number, especially in endemic areas Together with this, there should be a decrease in the number of nonspecific fibrocaseous granulomas reported

As a result of the above survey we feel strengthened in our belief that all solitary pulmonary lesions should be excised and pathologically examined The risk of thoracotomy is less than 1% (no mortality in this series) as compared to a death rate three times the expected for patients harboring a coin lesion Fully, densely calcified lesions are an exception to this rule as is a lesion which was recently stressed in the literature, a pulmonary hematoma which appeared as a coin lesion[16] In these latter lesions there is the history of trauma, and resolution of the lesion can be expected in a short time, although sometimes several months for complete disappearance is required We believe that with a proper history a possible hematoma may be safely observed for six to eight weeks, in which time resolution should be evident Failure to show such change is definite reason for thoracotomy in order to establish an accurate diagnosis

Summary

A series of 95 cases of solitary, circumscribed pulmonary lesions is presented and analyzed with respect to age, calcification, location, and skin test results The need for thoracotomy to establish a positive diagnosis in almost all cases is stressed The presence of calcium is regarded as a good sign of benign condition but is not proof of the innocuous nature of the lesion

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NOTE The opinions contained herein are those of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large

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PROFESSOR OF HISTORY OF MEDICINE –So far as I can see the first man who might be considered a professor of the history of medicine in America was Robley Dunglison, who was called to the University of Virginia in 1825 Thomas Jefferson, then Rector of the university insisted that he should teach to the best of his ability and with due diligence the history of the progress and theories of medicine But since the terms of his appointment foresaw that he should in addition teach anatomy, surgery, physiology, *materia medica,* and pharmacy we can hardly consider him a full-time professor of medical history His lecture notes were published by his son in 1872 and became a well liked textbook on the subject H E Sigerist, On the History of Medicine New York, MD Publications, Inc, 1960, page 234

ROUTINE TREATMENT OF TETANUS

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About 300 patients with tetanus have been seen in 25 years at the Cook County Hospital. Formerly the patients were mostly children, the treatment included sound proof rooms, subdued lighting, and heavy sedation with barbiturates. In the past 10 years the patients have been mostly adults, with heroin addicts predominating, treatment has been improved by the use of meprobamate to control the spasms evoked by somatic stimuli and the use of better respiratory care. The mortality of tetanus in heroin addicts has remained high (about 70%). The use of hypothermia in this type of patient has decreased morbidity and increased survival time, but it has not yet greatly decreased mortality.

In this era of rapidly advancing medical knowledge, with new and more potent drugs available and with ingenious new techniques developed to cure previously intractable diseases, it is surprising how little the basic principles of the treatment of tetanus have changed. Certainly, there have been advances over the years in the management of these patients, but they have consisted primarily of refinements of older techniques and the use of less toxic or more potent sedative drugs. The active management of the patient with tetanus still remains essentially symptomatic.

The efficacy of a new treatment regime for tetanus may be difficult to evaluate since many factors enter into the prognosis other than the treatment per se. For instance, the general health and hygiene of the patient is an important factor. Those patients who are infirm or aged, or who have a complicating sepsis or narcotic addition have a worse prognosis than those not so affected. In a given patient with tetanus the prognosis is much more dependent on the rapidity of onset of generalized spasms after the first symptom than on any other single clinical factor. In patients in whom generalized spasms appear within 24 hours after the first symptom (such as backache, stiff neck, and trismus) the mortality is over 80%, regardless of the treatment used. In those in whom this onset period lasts more than five days, the mortality is under 10%, even with little or no treatment. Unless these factors are taken into account, one might innocently and erroneously attribute curative powers to a new treatment.

During the last 25 years, in the tetanus service at the Cook County Hospital many types of treatment have been used. The regimen described herein is used currently and is based on experience with about 300 patients seen during this period. When the tetanus service was initiated in 1933, most of the patients were infants and children. In the last 10 years most of the patients have been adults, and most of these have been heroin addicts. The decrease in the incidence of pediatric cases is probably due to the general routine use of tetanus toxoid immunizations in the United States for infants and young children. Also, the routine use of tetanus toxoid in military inductees probably explains the recent prevalence of female patients in the adult population with tetanus.

Although the tetanus service team is captained by the chief of the Neuropediatric Service, there is active participation by the departments of medicine, pediatrics, surgery, anesthesiology, otolaryngology, physical medicine, biochemistry, and bacteriology. Members of the team are on a 24-hour "on call" basis with the active day-to-day care of the patient under the supervision of the neuropediatric attending physician and the residents in the departments of pediatrics, medicine, and surgery. The members of this team are responsible for making or corroborating the diagnosis of tetanus as well as for the actual management of the patient.

Although the mortality in tetanus is related to a number of factors, some beyond the control of the physician, there are others which he can influence. In large measure, the success of a tetanus service depends on the competence and devotion of the nursing staff. It is imperative to have 24-hour nursing available by nurses who have been instructed in many special techniques, particularly those related to respiratory and tracheotomy care. Routine instructions for the general care of tetanus patients and the specific instructions for the given patient are posted in the special room used for such patients. For purposes of simplification, the measures employed in the routine management of tetanus have been divided into several categories.

General Measures

Intelligent nurses, trained in respiratory care by anesthesiologists, are a very necessary part of the

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treatment of patients with tetanus The nurse must be able to recognize and to understand new and often subtle signs of impending complications and be prepared to meet emergencies as they arise

The time-honored use of a quiet, dark room is advisable but no longer necessary since meprobamate can be injected A bed board is placed beneath the mattress to give a more firm support for the patient s back On admission, all patients have a tap water enema after the necessary emergency procedures have been carried out This is to remove fecal impactions, collections of flatus, and other possible causes of visceral irritation from the rectum and colon Such visceral stimuli often trigger generalized spasms

Cultures are made of those wounds which are suspected of being the portals of entry of Clostridium tetani with use of anaerobic culture mediums This should be done before the patient receives any antibiotic therapy

Care of the Wound—Although some controversy still exists with regard to the necessity for radical or even mutilating surgery, it is our policy to excise small wounds when possible For those patients who have numerous lesions, any or more than one of which might be a portal of entry, incision and drainage (multiple, if necessary) are carried out All grossly infected lesions are débrided as widely as possible It is often impossible to débride all lesions or to identify the portal of entry in the patients who are heroin addicts, because many have administered their own shots intravenously as well as subcutaneously

Care of the wound afterward is then directed at controlling infection with use of antibiotic therapy and keeping the wound open to air by the use of compresses and oxidizing solutions The latter retard the growth of Cl tetani since it is an anaerobic organism Undiluted hydrogen peroxide or a 1 4,000 dilution of potassium permanganate is used routinely to irrigate the wound at least three times daily

Tetanus Antitoxin and Toxoid—Since tetanus antitoxin will not neutralize any toxin already fixed in the central nervous system, its use is aimed at neutralizing only circulating toxin which is not so fixed After an initial negative intradermal test for serum sensitivity (using 0 1 cc of 1 1,000 dilution of antitoxin), 40,000 units of the serum is given intramuscularly and an additional 40,000 units is given intravenously The intravenous antitoxin is diluted in 250 cc of isotonic sodium chloride solution to which 1 cc of 1 1,000 dilution of epinephrine has been added With doses of this magnitude, the antitoxin titer of the blood remains at protective levels for several months

In the event that serum hypersensitivity exists, as indicated by a positive intradermal test, with marked pseudopodium formation, or if there is a history of sensitivity to horse serum, antitoxin made with bovine serum should be used If bovine serum is unavailable, or if sensitivity to this serum also exists, antitoxin (equine) is given by the desensitization technique as follows Subcutaneous injections are given at 15-minute intervals in graduated increasing doses, as 0 1, 0 2, 0 4, and 0 7 cc of a 1 1,000 dilution, 0 1, 0 2, 0 4, and 0 7 cc of a 1 100 dilution, 0 1, 0 2, 0 4, and 0 7 cc of a 1 10 dilution and 0 1, 0 2, 0 4, 0 7, and 1 0 cc of undiluted antitoxin

After 30 minutes, the undiluted antitoxin is injected intravenously at 20-minute intervals, in ascending doses of 0 1, 0 2, 0 4, 0 7, and 1 0 cc If no untoward reaction has occurred, it is assumed that desensitization has been attained and the total dose of toxin-antitoxin (T A T) is slowly given as described, 40,000 units intramuscularly and 40,000 units intravenously As an additional precaution, however, 0 5 cc of a 1 1,000 dilution of epinephrine and 25 mg of promethazine hydrochloride are given subcutaneously prior to the intravenous injection

If any of the previously mentioned desensitizing injections are followed by respiratory distress, edema, urticaria, or any other symptoms of serum hypersensitivity, the next dose is not increased, but the same or smaller dose than that which caused the difficulty should be repeated after an interval of 30 minutes If reactions occur while the tetanus antitoxin is being given intravenously, the injection should be temporarily stopped and a 1 1,000 dilution of epinephrine should be slowly given intravenously, in a dose of 0 5 to 1 0 cc and repeated in a few minutes if required In addition, promethazine hydrochloride (25 mg) is given intravenously Cortisone may also be added, in a dose of 25 to 50 mg every six hours Both cortisone and promethazine hydrochloride may have to be continued for several days These are adult doses of medication and are reduced proportionately for children

Since tetanus antitoxin confers only passive immunity, tetanus toxoid is also given in order to stimulate active immunization Our experience with two patients who had recurrent tetanus confirms the fact that having the disease does not result in immunity to it Generally, the first dose of 0 5 cc of alum-precipitate tetanus toxoid is given intramuscularly at the end of the first week and repeated in about one month, with third and fourth doses at monthly intervals thereafter

The titer of tetanus antitoxin in the blood, after doses of 10,000 units or less of antitoxin, does not interfere with the formation of active antibodies by injection of toxoid[1] With the relatively high dosages of tetanus antitoxin that we use (80,000 units), there may be some interference with the development of active immunity by toxoid for several months[2] From a practical viewpoint, therefore, in the absence of specific data on how long such antibody formation will be delayed, we have given our first dose of toxoid on the seventh day, because its injection is without deleterious effects and the development of passive immunity from toxoid, even in the presence of high concentrations of antitoxin, may vary with different patients To be certain, however, a fourth or even a fifth dose of toxoid should be given one to two months after the third dose

Antibiotics—Penicillin, the most effective antibiotic for killing or inhibiting the growth of Cl tetani, is given intramuscularly as procaine penicillin in a dose of 600,000 units daily or intravenously as aqueous penicillin in a dose of 400,000 units three times daily Broad-spectrum antibiotics, such as tetracycline, are also given for control or prevention of complicating infections The usual dose is 500 mg every six hours for adults and appropriately smaller doses for children The choice of antibiotics for secondary infections may be modified as indicated by culture and sensitivity studies They are used particularly to prevent the respiratory infections that are incident to tracheotomy, as well as to combat complicating pyogenic infections elsewhere

Respiratory Care

One of the most important aspects of the total care of the patient with tetanus is the provision of a patent airway It is mandatory More deaths are caused by the respiratory complications of tetanus than by tetanus per se

Respiratory embarrassment in tetanus may occur as a result of several mechanisms, each of which requires prompt attention Spasms of the respiratory muscles, including laryngospasm, may occur as part of the general spasms of skeletal muscles and must be relieved Respiration may also be embarrassed by spasms of the extensor muscles of the back and of the abdominal muscles, which interfere with normal breathing Later in the course of the illness there is the additional danger of aspiration pneumonia, or, of the airway is plugged with mucous and other secretions, of secondary atelectasis In the most severe forms of tetanus, such as occur in heroin addicts, a bulbar or central type of respiratory failure may occur which is usually associated with respiratory and cardiac dysrhythmias

To provide a patent airway, tracheotomy should be carried out routinely on all severely ill patients, all those with a rapid onset of seizures (occuring in less than 36 hours), and as a special group, all those with heroin addiction Tracheotomy is no longer done routinely, though it may be done, if necessary in mild cases, when seizures are absent or infrequent, or in infants

The tracheotomy is performed by the otolaryngologist in the standard manner After sterile preparation and draping, a skin incision is made under local anesthesia, and the tracheotomy tube is inserted through a "window" in the second tracheal cartilage It is anchored to a muslin band around the patient's neck A relatively large tube, no 2 to 4 for children or no 6 to 8 for adults, is used Several spare sterile tracheotomy tubes are kept by the bedside

The proper care of the tracheotomy tube is very important and calls for experienced help Although many lives are saved by providing a patent airway, the tracheotomy adds some inherent complications, primarily those caused by bronchial obstruction by plugs of mucous engendered by the tube Routinely, the tracheobroncial tree is suctioned frequently, at least once an hour, to keep it free from secretions For aspiration, blunt-tipped coudé catheters of relatively large gauge, compatible with the size of the tracheotomy tube, are used A supply of clean catheters sterilized in a 1 2,000 dilution of zephiran chloride is kept at hand so that a fresh catheter may be used for each aspiration Moderate suction (100 to 200 mm Hg) is used for brief periods of about 15 seconds, and the catheter is introduced into both main stem bronchi by tilting the patient's head and body or by rotating the tracheotomy tube The inner cannula is removed and cleaned hourly The outer cannula is changed daily or at least every second day, since many otherwise unrecognized mucous plugs form about the outer cannula The patient is turned from side to side frequently (at least hourly) to promote more efficient drainage In order to thin the tracheobronchial secretions, 2 to 4 cc of isotonic sodium chloride solution is instilled directly into the tracheotomy every 30 to 60 minutes Emulsifying agents (As Alevaire) are also used, either as aerosols or by addition in 25% concentration to the instilled isotonic sodium chloride solution Bronchoscopy, if necessary, can be carried out through the tracheotomy incision

For patients who are unable to maintain adequate ventilation, oxygen is added as indicated At times, mechanical respiratory aids must be used, particularly if respiratory paralysis has been induced with curarization Automatically cycling positive pressure respirators (as the Morch Piston Respirator) can be attached directly to the tracheotomy tube This insures a constant respiratory rate and rhythm, and by varying the amount of positive pressure applied, insures a constant exchange of air This is much more effective than negative pressure devices For adults, the respiratory rate is usually set at about 15 cycles per minute, the pressure setting is regulated to provide an exchange of 1,500 to 2,000 cc of oxygen per stroke For children, a more rapid rate (20 to 22 per minute) and a smaller exchange (500 to 700 cc) is used In curarized patients, hyperventilation is induced, since the respiratory alkalosis which ensues seems to have a paradoxical mild sedative effect in the presence of curarization

Maintenance of Nutrition—For the first 12 to 24 hours, and even longer if deemed advisable, fluids are given intravenously and no attempt is made to feed the patient otherwise For adults, the average 24-hour fluid and electrolyte intake is supplied as 2,000 cc of 5% dextrose with water and 1,000 cc of isotonic sodium chloride solution to which 200 cc of 2% of potassium chloride solution is added This intravenous setup is also used as the vehicle for the delivery of the intravenously given tetanus antitoxin and any other medicament given intravenously For patients who are maintained on intravenously given fluids for over 24 hours, daily blood studies should be made, including hematocrit reading and determination of levels of serum sodium, potassium, and chloride, carbon dioxide combining power, total protein level, and urea nitrogen level Urinalyses, including the determination of the total urinary volume and specific gravity, should also be done daily If veins for percutaneous puncture are inaccessible, as is often the case in heroin addicts or small infants, a surgical cut-down is done on any such accessible vein as the saphenous at the ankle or thigh, or, if necessary, the femoral After the patient's general condition has stabilized, the intravenously given fluids are decreased or discontinued At this time, gavage feedings are begun by nasogastric tube and are continued until trismus is decreased sufficiently to allow oral feedings The food given by gavage is essentially a high-protein, high-calorie concentrate prepared with 12 eggs, 250 Gm of dextrin-maltose mixture (Dextri Maltose No 1), 300 Gm of a powdered food supplement, (Meritene), 1,350 cc of milk, 450 cc of orange juice, and sufficient water to bring it up to 2,500 cc

The 24-hour intake for an average adult patient is 2,500 cc of this high-protein feeding, plus 600 cc of orange juice to supply additional potassium, and 600 cc of water or dextrose in water The feedings are divided into 12 portions given every two hours and consisting of about 220 cc of high-protein mixture, 50 cc of orange juice, and 50 cc of water at each gavage This supplies about 3,600 cc of fluid daily and between 4,000 and 5,000 calories, with minimal vitamin requirement and adequate electrolytes In addition, supplemental doses of the B complex vitamins are given

General Hygiene—If the patient is unable to void spontaneously after such methods as warm, wet cloths applied to the genitalia have been tried, catheterization must be resorted to and should be repeated every six to eight hours as necessary The use of an indwelling catheter is inadvisable, as this, almost without exception, triggers continuous severe seizures in severely involved patients

If repeated catheterizations are necessary for a period of days (a most unusual occurence), the advisability of a suprapubic cystostomy should be considered Usually, patients are able to void spontaneously by the end of their first 48 hours of hospitalization

The problems related to the gastrointestinal tract are mainly those of gaseous distention and constipation Since even these relatively trivial complaints may precipitate violent seizures, attention must be paid to them The use of rectal tubes and tap water enemas for constipation and gaseous distention are usually sufficient Cathartics and neostigmine bromide drugs (Prostigmin) are not used since visceral pain induced by such drugs also may trigger seizures Fecal impactions are treated by digital manipulation Carminatives, such as tea or peppermint water, and stool softeners, such as dioctyl sodium sulfosuccinate (Colace) given orally or mineral oil given rectally, are safe and often effective

Control of Spasms

The control of spasms is the crux of the management of the patient with tetanus It has constituted one of the most difficult and unsatisfactory aspects of therapy The control of seizures is based upon the use of several general classes of drugs, either sedatives, anesthetics, skeletal muscle relaxants, or myoneural transmission inhibitors, used either alone or in various combinations Over the years many drugs have been tried, including the barbiturates, tribromoethanol (Avertin), curare and its analogues, mephenesin and its analogues, and some of the newer muscle relaxants Practically all have been abandoned

Our present drug of choice for the control of seizures in tetanus is meprobamate given intramuscularly[3] It has proved to date to be the most astonishing antispasmodic for tetanus It effectively abolishes seizures which are triggered by such somatic stimuli as pinprick, loud noises, and flashing lights It will not, however, affect the seizures which are triggered by visceral stimuli such as a distended bowel or bladder, a catheter in the urinary bladder, mucus in the tracheobronchial tree, or fecal impaction, nor will it affect seizures triggered by proprioceptive stimuli which are evoked by turning the patient or by gross movement of his large joints

Since spasms due to somatically induced stimuli are abolished by this drug, the persistence of seizures after meprobamate is given is a signal to the physician to search for a visceral cause and to attempt to correct it Unlike sedative drugs that control seizures only at the expense of deep depression of the patient (analogous to the analgesic action of morphine which masks the symptoms of a ruptured appendix), meprobamate, by its selective action, permits the patient to be awake and communicative Often, a distended bladder, a fecal impaction, or some mucus in the tracheobronchial tree will be found to be the offending stimulus if spasms persist

Injectible meprobamate (Miltown) is supplied in a 5 cc ampul containing 400 mg of meprobamate in polyethylene glycol (80 mg per cubic centimeter) In adults, the dose is 400 mg every three to four hours as needed to control seizures The effective dose in children over the age of 5 years is about 200 to 300 mg and in infants under 2 years, 50 to 100 mg Since the drug is extremely safe, without any dangerous side-effects, there need be no hesitation in clinical titration of the dose for a given patient by trial and error Surprisingly, these relatively large intramuscular injections are not painful, since meprobamate apparently has a local anesthetic effect Orally administered meprobamate is not effective for the control of spasms in the active or severe stages of tetanus but may be useful in the convalescent or mild cases in doses of 400 to 800 mg every four hours We have used several of the other currently available drugs which have a muscle relaxant effect, but none have had nearly the dramatic effect as that induced by intramuscularly given meprobamate

For the patient who continues to have unexplained spontaneous spasms after the administration of meprobamate, in whom the visceral triggers cannot be identified or corrected, chlorpromazine hydrochloride in a dose of 25 to 50 mg given intramuscularly every three to four hours (for the adult) is added This drug is more effective than meprobamate in reducing spasms due to visceral causes but has a definite undesirable depressing and soporific effect If given over a period of several days, it also tends to lower the blood pressure to dangerous levels For this reason it is advisable to add promethazine hydrochloride in doses of 10 to 25 mg to each dose of chlorpromazine

For the patient who continues to have seizures despite the use of meprobamate and chlorpromazine, a barbiturate such as sodium phenobarbital or pentobarbital is added, being given intramuscularly in a dose of 100 to 200 mg (1½ to 3 Gm) every three to four hours, as necessary The barbiturates cause a marked depression of the sensorium and the danger of respiratory embarrassment must be carefully avoided Used in conjunction with meprobamate and chlorpromazine, the average daily requirement for barbiturates to control spasms has dropped markedly from an average of 1,400 to 1,800 mg to 200 to 400 mg per day Generally, barbiturates are now used only sparingly, primarily for night-time sedation and sleep One of the rapidly acting barbiturates may also be given orally or per stomach tube in a dose of 100 to 200 mg as indicated

The Addict

Heroin addicts presently comprise the single largest group of patients with tetanus seen at the Cook County Hospital Not only do these patients generally suffer tetanus in its most severe form, but they also are handicapped by poor hygiene, poor nutrition, avitaminosis, and other physical and emotional problems The course of the disease is fulminant, with bulbar symptoms, including cardiorespiratory dysrhythmia and hyperthermia Since the death rate in this group is so high, special measures are justified in an attempt to reduce morbidity and mortality

To prevent withdrawal symptoms, since heroin is legally unavailable, the patient is given methadone hydrochloride in doses of 5 to 10 mg every three to four hours This dose is empirical, since it is generally impossible to learn the exact dose the addict was taking in view of the narcotic supplier's practice of adulterating or diluting his wares Since these patients often have multiple abscesses at sites of injection, thorough débridement may be impractical, and therefore antibiotic therapy is used more frequently Percutaneous canalization of a vein may also be impossible, because of local infections and obliteration of all available subcutaneous veins, so that cut-downs, to enable intravenous administration, are more frequently necessary

Tracheotomy is routinely done, even if the patient is seen during the early stages of the disease, since experience has taught that within 12 to 24 hours there will probably be spasms and respiratory embarrassment

In spite of all precautions and the use of meprobamate, chlorpromazine hydrochloride (Thorazine), and barbiturates, the mortality of tetanus in heroin addicts has remained inordinately high (about 70%) so that hypothermia has recently been employed in an attempt to reduce the metabolic needs of the patient and the rate of growth of secondary inflammatory organisms This regimen has definitely decreased morbidity and has substantially increased survival time but has not yet greatly decreased mortality However, since most of our deaths from tetanus can now be attributed to pulmonary, cardiac, or septic complications, it may be possible with more experience with hypothermia and its influence on the effect of other drugs administered, as well as on the reactivity of the patient, to reduce the mortality substantially Certainly our present regimen enables us to identify the complications more readily and to recognize our own ineptitudes and errors more clearly

The techniques of hypothermia will not be discussed here except in general outline Hypothermia is achieved by means of a water blanket with constantly circulating cold tap water Drugs are used to facilitate hibernation The "lytic cocktail" consists of methadone, 10 mg, chlorpromazine, 50 mg, and promethazine, 50 mg, as the initial intramuscular dose This combination, along with the external cooling, is ordinarily adequate to lower the temperature rather rapidly to 94 to 96 F (34 to 35 C) rectally and then, more slowly to the desired level of 84 to 88 F (29 to 31 C) The patient is then maintained at this temperature by repeating the lytic cocktail at 8-to-12-hour intervals, as it is needed

The temperatures are recorded electronically by an indwelling rectal electrode

The major difficulty encountered in lowering the temperature below 94 to 96 F is shivering, which in turn, tends to raise the temperature To overcome this, it may be necessary to use an anesthetic or one of the curare derivatives (preferably one of the faster acting ones such as dimethyl tubocurarine chloride) by continuous intravenous administration When curarization is used it becomes necessary to use a positive pressure respirator connected directly to the tracheotomy tube As indicated previously, hyperventilation of the patient is used to increase sedation

Convalescence

When the patient's clinical status is such that he no longer has gross respiratory difficulties, consideration is given to the early removal of the tracheotomy tube The tube is first plugged for short periods and then for longer periods, accordingly as the patient is able to tolerate it When the tracheotomy can be completely occluded for a minimum of 24 hours, it may then be removed

Antibiotic therapy is usually discontinued after five to seven days, unless some intervening complication has occurred which requires its continuance Gradually the dosage of intramuscularly given meprobamate is reduced and then discontinued, it is replaced by orally given meprobamate in a dose of 400 to 800 mg every four hours At this time, also, the patient should begin physical therapy and ambulation Before weight-bearing is allowed, roentgenograms in both the anteroposterior and lateral views should be made of the entire spine to rule out the existence of a possibly unrecognized compression fracture or subluxation due to prolonged severe seizures

Bearing in mind that the recovery from a clinical attack of tetanus does not confer immunity, it is also necessary to carry out active immunization The first dose of tetanus toxoid, given on the seventh day after entry, is followed by at least three more such injections given at monthly intervals

The foregoing outline of the therapy of tetanus used at Cook County Hospital is intended primarily as a guide At times, other medicaments which are not mentioned might be indicated, for instance, cortisone during periods of shock Dosages given are primarily for adults, but all of them need to be tailored to the given patient As in all fields of medicine, the doctor must make the final decision as to what is indicated in a given case Common sense still remains the most important ingredient

Summary

The routine treatment of tetanus at the Cook County Hospital, in addition to general measures, consists primarily of heavy doses of antitoxin, good nursing to prevent and manage respiratory complications, and the administration of meprobamate, chlorpromazine (Thorazine), hydrochloride, and barbiturates, in that order

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The Morch Piston Respirator used in this study was supplied by V Mueller and Company, Chicago

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FAMILY HEALTH PROGRAM —The Family Health Program will serve a group of families in the neighborhood of the [Massachusetts General] Hospital, acting as family physician for those who enroll Medical and nursing care will be provided at home, in the Clinics, or in the Hospital The enrolled families will be asked to pay as much of the cost as they can The principle objective of this new service is to furnish its families the most up to-date, comprehensive medical care, both preventive and therapeutic, that medical science now knows how to provide The interest of the Rockefeller Foundation is to give an opportunity to Harvard Medical students to participate in such a comprehensive scheme of medical care It is planned to invite fifteen first-year and fifteen third-year students to work in the Family Health Service and to follow, during their entire medical school career, the one or two families assigned to them This arrangement, it is felt, will give the students an idea of the personal and environmental, as well as the medical problems of patients and thus better prepare them to be practicing physicians —N W Faxon The Massachusetts General Hospital 1935-1955, Cambridge, Mass, Harvard University Press, 1959, page 124

GRISEOFULVIN IN DERMATOMYCOSES

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Griseofulvin was administered orally in uniform doses of 1,000 mg. daily to 80 patients with dermatomycoses due to Trichophyton mentagrophytes, Trichophyton rubrum, Candida albicans, Epidermophyton floccosum, and Microsporum lanosum. Studies of blood and urine were made at four-week intervals. Six of the ten patients with gastrointestinal side-effects were forced to stop therapy. Success of the medication varied with the site and fungus. Greatest success occurred in patients with rubrum tinea corporis and in those with onychomycosis due to T. rubrum and T. mentagrophytes. Acute dermatophytosis, especially of the soles, toe webs, and groin, showed less prompt response to orally given griseofulvin than to topical therapy. Dermatoses similar to fungus infections did not respond to griseofulvin.

This is a report of one year's clinical experience in the treatment of superficial fungus infections with the orally given antibiotic, griseofulvin. Riehl,[1] Williams, and others,[2] and Blank and Roth,[3] were the first to report preliminary results in treating fungus infections in human beings. Since then, other reports concerning observations on griseofulvin therapy have appeared in the literature.[4]

Method of Treatment and Results

Our study consisted of 80 private patients treated with griseofulvin for various dermatomycoses. Each patient had a uniform dosage of 4 tablets daily, or 1,000 mg., daily. A 250-mg. tablet was taken after each meal and one at bedtime. Prior to therapy patients were questioned with regard to general health, previous serious illness, and penicillin reactions. The hematological examination in 35 of the 80 patients treated comprised erythrocytometry, leukocyte count, measurement of hemoglobin level, and differential blood cell count. Urinalyses for albumin and glucose were done for each patient. At intervals of four weeks, during therapy, both blood studies and urinalyses were repeated. Potassium hydroxide preparation of the material scraped from the involved site was examined under the microscope for the presence of fungi. Cultures with Sabouraud's medium were also made prior to treatment. Fungus examinations were made at intervals of two to four weeks during griseofulvin therapy.

Since there was considerable variation in the response to medication of the various sites of mycotic involvement, the results are given according to the site involved. Patients with multiple sites involved are indicated in the tables.

The results of treatment are indicated in the following manner: "cleared" indicates clinical absence of signs of fungus infection and no fungus found by direct microscopic inspection or by culture, "improved," definite objective clinical improvement in the appearance of lesions but fungus could be demonstrated, "unimproved," no clinical improvement observed, and those cases in which side-effects, inadequate length of observation, or loss to follow-up examination necessitated removal from the tabulated results are designated "dropped."

Dermatomycoses

Onychomycosis.—Of 36 patients who had fungus infection of the nails, 16 had infection of the fingernails and toenails. Table 2 shows the results. The one case of Trichophyton mentagrophytes infection of the nail cleared after five months of 1,000 mg. daily doses of griseofulvin. There was no recurrence in this case three months after treatment was stopped. Among the seven improved patients who had T. mentagrophytes infection, one had to stop therapy after five months because of nausea and flatulence. The other six have made good progress with involvement and positive cultures still present only at the distal portion of the nail. At the time of this writing each patient had had at least four months of medication and was continuing therapy.

The four patients who had Trichophyton rubrum infections which were clinically cured and had cultures that gave negative results had medication for three, four, six, and eight months, respectively. A patient who had four months of therapy had a recurrence of T. rubrum infection three months after it was ceased. The five patients whose cases of T. rubrum infection improved had medication for a minimum of five months. At the time of this writing all were continuing with therapy. One patient has had therapy for 11 months, the condition of the involved toenails has improved, but cultures still give positive findings.

The two patients who had unimproved cases of Candida albicans infection did not respond to medication of three months' duration.

Tinea Corporis—The patient who had a cleared case of tinea corporis with T mentagrophytes infection of the legs and abdomen was a 62-year-old man No recurrence had been noted four months after stopping therapy of three months' duration Three patients with generalized T rubrum infection responded promptly to therapy In the first patient, all lesions disappeared two weeks after onset of therapy Treatment has continued for eight months as fungus involvement of the nails was still present The second case with fungus involvement of the trunk and lower extremities of four years' duration cleared after three weeks of therapy No recurrence has been noted for the four months since therapy terminated In this case, infection of the nail had persisted The third case of T rubrum infection cleared after two weeks of therapy Medication was continued but had to be stopped after three weeks because of side-effects No recurrence has been seen for five months after medication was discontinued All of these patients, in addition, had T rubrum infection of the toenails The infection of the toenails has persisted

TABLE 1—*Fungi Found in Eighty Private Patients*

	T menta graphytes	T ru brum	C albi cans	E floc cosum	M fe lineum	Patients Total No
Onychomycosis	19	11	6	0	0	36
Tinea corporis	1	3	1	0	0	5
Tinea pedis	24	5	4	0	0	33
Tinea of hands	1	1	3	0	0	5
Tinea inguinalis	1	0	3	1	1	6

Tinea Pedis—Table 2 shows the results of treatment in patients with tinea pedis Extensive chronic T mentagrophytes infection of the soles completely cleared in one patient after two months of therapy No recurrence has been noted after six months Improvement was noted in 11 patients, and 4 patients with T mentagrophytes infection had no improvement The four cases unimproved with griseofulvin were all in the acute stage, the patients had tender pruritic patches of vesicles on the soles and toes In two of these cases there was an increase in the involvement and symptoms during griseofulvin therapy The three cases of T rubrum infection were cleared within six weeks of griseofulvin therapy The one improved patient had a positive culture after eight weeks of therapy Medication was continued No response to medication was noted in the two infections with C albicans

Tinea of the Hands—Table 2 shows the results of treatment in cases of tinea of the hands Of the eight patients, one case of T mentagrophytes and one of T rubrum infection cleared with griseofulvin therapy Improvement has been noted in the two patients with T mentagrophytes and in the one with T rubrum infections There was no response to medication in the two cases of C albicans

Tinea Inguinalis—Table 2 shows the results in patients with tinea inguinales One case of Microsporum lanosum infection of the pubic hair in a 34-year-old woman was cleared with 1,000 mg of griseofulvin daily for six weeks There has been no recurrence four months after therapy was stopped The Epidermophyton floccosum infection cleared in three weeks of therapy No recurrence has been noted five months after therapy had been stopped

Side-Effects

Of the 80 patients treated with griseofulvin, 35 had at least three complete blood counts at intervals of four weeks during therapy There were no discernible changes in the amount of hemoglobin, erythrocytes, or leukocytes nor in the differential leukocyte percentages Urinalyses for these same 35 patients gave normal findings, also at intervals of four weeks during therapy

Gastrointestinal symptoms were the predominant side-reactions to griseofulvin One or more of the following symptoms were present in those who had them nausea, eructation, diarrhea, and flatulence Of the 80 patients, 10 (12%) had these symptoms In the 10 patients with gastrointestinal symptoms, 6 had to stop therapy entirely after one or more interruptions in treatment for four to five days Onset of symptoms varied from the first week of to five months after the start of therapy Three patients had transitory headaches, however, therapy was continued, and no further disturbances were noted

TABLE 2—*Results of Treatment by Type of Fungus Infection*

	Patients No				
Causative Organism	Cleared	Improved	Unimproved	Dropped*	Total
Onychomycosis					
T mentagrophytes	1	7	1	10	19
T rubrum	4	5	0	2	11
C albicans	0	0	2	4	6
Total	5	12	3	16	36
Tinea Corporis					
T mentagrophytes	1	0	0	0	1
T rubrum	3	0	0	0	3
C albicans	0	0	0	1	1
Total	4	0	0	1	5
Tinea Pedis					
T mentagrophytes	1	11	4	8	24
T rubrum	3	1	0	1	5
C albicans	0	0	2	2	4
Total	4	12	6	11	33
Tinea of Hands					
T mentagrophytes	1	2	0	0	3
T rubrum	1	1	0	0	2
C albicans	0	0	2	1	3
Total	2	3	2	1	8
Tinea Inguinalis					
T mentagrophytes	0	0	0	1	1
M lanosum	1	0	0	0	1
C albicans	0	0	2	1	3
E floccosum	1	0	0	0	1
Total	2	0	2	2	6

*Side-effects and inadequate treatment

Two patients developed pharyngitis Resumption of griseofulvin therapy, after two weeks' pause in therapy, brought about a recurrence of the pharyngitis Another patient developed polyuria and nocturia, which he ascribed to griseofulvin, however, after resumption of griseofulvin, there was no recurrence of symptoms

Three patients with known previous allergic reactions to penicillin had no difficulty with griseofulvin therapy One patient with no history of penicillin allergy developed urticaria, predominantly on the lower extremities, after four months of 1,000 mg of griseofulvin daily There has been no recurrence of urticaria since the medication was stopped Therapy with griseofulvin has not been resumed because of the patient's reluctance He also had gastrointestinal symptoms

Comment

On the basis of one year's use of griseofulvin, it is apparent that a period of several years will be necessary for a complete evaluation of the efficacy of this drug In the treatment of superficial mycotic infections, with the exception of tinea capitis, relapse can be expected when the medication is stopped This would seem to indicate that immunity is not produced by griseofulvin therapy Reappearance of clinical symptoms indicate resumption of therapy

Acute dermatophytosis of the feet, especially the toe webs, does not respond readily to griseofulvin therapy Topical medication produces a much quicker response to the symptoms accompanying the acute phases of dermatophytosis, on the toe webs, inguinal region, or elsewhere

Dermatophytosis caused by C albicans does not respond to griseofulvin therapy, therefore, it is important to identify the causative fungus by cultures before prolonged therapy is embarked on

It was noted that in all of the cases of onychomycosis of the fingernails there was also fungus infection of the toenails All four patients with tinea corporis had toenail involvement, and two of the four had, in addition, fingernail fungus infections Relapse in patients with tinea corporis may be expected if nail infection is present after therapy is stopped

One patient had eosinophilic granuloma and T rubrum infection of the soles and toes, a case similar to that reported by Lewis and Cormia[4] Griseofulvin, 1,000 mg daily for three months, produced no change in the violaceous nodule, 2 cm in diameter, over the left malar prominence in our patient This seems to confirm Lewis's and Cormia's belief that the T rubrum infection was a coincidental finding in a case of eosinophilic granuloma

The specificity of this drug excludes not only C albicans infections but also other dermatoses Because of the dramatic response of specific dermatomycoses, we were tempted to treat empirically several dermatoses that in some way were similar to fungus infections Five cases of recalcitrant pruritus ani and vulvae, two cases of pustular bacterids, four cases of psoriasis, and eight cases of persistent dyshidrotic dermatitis of the hands have not responded to griseofulvin therapy Psoriasis of the nails in three patients showed no response to griseofulvin One patient with a typical case of psoriasis of the nails and the body also had a T rubrum infection of the toenails This 11-year old boy responded well after two months of therapy, however, there has been no improvement in the psoriasis

The most heartening aspects of this study have been the remarkable clearing of T rubrum infections in tinea corporis and the clearing of onychomycosis due to T rubrum and T mentagrophytes Hitherto, both types of infection have responded poorly, if at all, to topical treatment

Summary

Eighty patients with dermatomycoses caused by Trichophyton mentagrophytes, Trichophyton rubrum, Candida albicans, Epidermophyton floccosum, and Microsporum lanosum were treated with griseofulvin There were 36 cases of onychomycosis, 5 of tinea corporis, 33 of tinea pedis, 8 of tinea of the hands, and 6 of tinea inguinalis Dramatic response to griseofulvin was noted in patients with onychomycosis and tinea corporis, excluding those caused by C albicans Acute dermatophytosis, especially of the soles, toe webs, and groin, showed less prompt response to oral griseofulvin therapy than to topical medication Side-effects from griseofulvin therapy were noted in 12 (15%) of the 80 patients None was serious or irreversible after medication was stopped

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PERSISTENT MENACE OF PNEUMOCOCCAL MENINGITIS

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Prior to the use of the sulfonamides recovery from pneumococcal meningitis rarely occurred. Even after the sulfonamides had been thoroughly evaluated in this form of suppurative meningitis the mortality in different medical centers varied between 60 and 80%.[1] A further reduction in fatalities occurred after penicillin became available. In summarizing the experience with penicillin at the University of Minnesota Hospitals up to 1946, the mortality was found to be 23.5%, although the total number of treated cases was small, and about one-half of the patients were infants and children.[2]

The purpose of this communication is to summarize the results of the treatment of pneumococcal meningitis at the University of Minnesota Medical Center between Jan. 1, 1945, and July 1, 1959. During this period a total of 55 bacteriologically proved cases were treated. There is evidence that the number of treated cases was considerably greater, but many persons had been treated with antibiotics just prior to being transferred to the University Hospitals, and definitive bacteriological data could not be obtained under these circumstances. Although penicillin, with or without a sulfonamide, remains the most effective therapeutic agent, the present analysis reemphasizes the seriousness of pneumococcal meningitis in the adult over 50 years of age. Although penicillin has been used extensively for the treatment of upper respiratory infections, there is no evidence that strains of pneumococci have become penicillin-resistant.

Primary Source of Infection

Observations over a period of two decades on the pathogenesis of pneumococcal meningitis at the University of Minnesota Hospitals have revealed that pneumococcal pneumonia is not commonly the primary cause of meningitis. In the present series only 4 of the 55 patients had demonstrable infection of the lungs. On the other hand, 18 patients, or 32.7%, had otitis media, with and without mastoiditis. This was by far the most common factor with meningeal involvement. Infection of the parenasal sinuses appeared to be much less commonly present. Head injury preceded the appearance of meningitis in only four cases. No primary source of infection could be determined in 22 of the cases.

Treatment

Antibiotics.—Although some variations occurred in the doses of antibiotics that were used, 52 of the 55 patients received penicillin as the drug of choice.

In a series of patients with meningitis cared for over a period of 14½ years there were 55 in whom the causative organism was identified as a pneumococcus. The overall mortality rate was 25%, but in patients over 40 years of age the mortality rate exceeded 50%. Only 4 of the patients had a demonstrable infection in their lungs, 18 had otitis media, and this was the most common factor in meningeal involvement. In 22 patients no primary source of the pneumococcal infection could be found. The most common neurological complication was damage to the cranial nerves and resultant visual and auditory deterioration. Among five patients who had recurrent pneumococcal meningitis there were a 7½ year old boy who died during his 6th attack and a 39-year old woman who entered the hospital with her 15th attack and recovered. The treatment in 52 cases was penicillin given parenterally. There was no evidence of advantages in intrathecal injection. The authors suggest that sulfadiazine be given orally as long as penicillin is continued.

One patient lived only a short while after entry into the hospital and received no drug therapy. One patient lived only a day and was given sulfadiazine. Broad-spectrum antibiotics alone were administered to another patient, who recovered. Penicillin alone was administered to 11 of the patients, while 22 of the patients received penicillin and sulfadiazine, and 18 were given penicillin and broad-spectrum antibiotics. Chloramphenicol or tetracycline was frequently administered along with penicillin because the bacteriological cause of the meningitis was not clear during the initial phases of the illness.

During the first few years of this study patients with pneumococcal meningitis received penicillin intrathecally, as well as parenterally. From 10,000 to 20,000 units of penicillin were injected intrathecally. But with added experience, it was observed that high concentrations of penicillin appeared in the cerebrospinal fluid after large parenteral doses of the drug. Moreover, the intrathecal use of penicillin did not appear to alter the outcome of the patients, providing large parenteral doses were used.

During recent years, the treatment of pneumococcal meningitis has called for large parenteral in-

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jections of penicillin At least 1 million units per hour have been given intravenously After definite improvement has occurred, equivalent doses were given intramuscularly, that is, 4 to 5 million units every four to six hours This schedule has been maintained, in most instances, for a minimum of two weeks, and preferably three weeks It was recognized that if the doses of penicillin were reduced too abruptly, or treatment discontinued too early relapses occurred It is generally accepted that penicillin should be supplemented with sulfadiazine, in an adult dose of 4 to 6 Gm per 24 hours, and continued at least for as long as penicillin is administered

A patient presented occasionally with a history of sensitivity to penicillin Under these circumstances, sulfadiazine could be administered in the foregoing doses, along with 3 to 4 Gm of chloramphenicol or tetracycline per day In the present series of cases, one patient exhibited penicillin sensitivity after treatment had been started

Surgical Treatment of Primary Focus—In three patients, pneumococcal meningitis was associated with otitis media and mastoiditis In two girls, one 7 years old and one 13 years old, meningitis recurred shortly after chemotherapy had been concluded Recovery promptly took place, after mastoidectomy had been carried out in each of the patients In a third patient, a child 8 months of age, recovery was very doubtful as a result of antibiotic therapy A mastoidectomy was then performed, which was followed by improvement and recovery

Steroid Therapy—Since cortisone had been shown to subdue the inflammatory response of infection, this steroid was considered as a possible adjunct in the therapy of pneumococcal meningitis, in which inflammation of the meninges is highly undesirable In the present series five patients were treated with antibiotics and adrenocortical steroids The first patient (case 1, table 1) was treated in 1951 The patient was managed in this manner because she also had peripheral vascular failure She received a pressor drug (arterenol [norepinephrine]) as well Although she was desperately ill, she recovered We were somewhat reluctant to use the steroids in further patients because at that time it was not known what might happen to the host's defense mechanism This apprehension was dispelled by further experience, and by the favorable report of others[2] Only five patients have been treated with steroids and antibiotics, but all of the five did recover, and three were over 60 years of age

Steroid therapy should be further evaluated, especially in patients with peripheral vascular failure as a complication of pneumococcal meningitis It is recommended that 500 to 1,000 mg of hydrocortisone per day should be given intravenously, probably along with an appropriate pressor agent such as arterenol or metaraminol This amount of steroid given over a critical period of a few days has not caused any serious side reactions in other patients treated for bacterial shock This therapeutic approach has been beneficial in patients having pneumococcal pneumonia with peripheral vascular collapse[3]

Table 1—*Adrenocortical Steroids in Pneumococcic Meningitis*

Patient No	Age Yr	Sex	Clinical Features	Therapy	Outcome
1	66	Female	Otitis media coma shock, oliguria type 1 pneumococci	Penicillin—1 million units I V every 4 hr for 7 days 1 million units I M every 4 hr for another 8 days Arterenol—Cortisone—100 mg every 8 hr for 8 days	Recovery with scattered neurological changes
2	64	Female	Semistuporous no primary focus	Penicillin—300 000 units I M every 6 hr for 12 days Streptomycin—2 Gm every 12 hr for 3 days cortisone—100 mg I V then 50 mg every 6 hr for 5 days, 25 mg every 6 hr for 1 day	Recovery
3	5	Male	Nephrosis no primary focus	Penicillin—1 million units I V every 2 hr for 3 days sulfadiazine—450 mg orally every 6 hr for 7 days cortisone—12 5 mg orally every 6 hr for 9 days	Recovery
4	40	Male	Pneumococcic meningitis 10 yr previously with residual damage to 8th cranial nerve no primary focus in present attack	Penicillin—5 million units I V and I M daily for 15 days sulfadiazine—1 Gm daily for 15 days, hydrocortisone—100 mg I V daily for 7 days	Recovery
5	39	Female	Irrational and febrile 13th attack of pneumococcic meningitis type 29 pneumococci present attack	Penicillin—1 million units I V 2 times daily for 9½ days 2 million units I M every 6 hr for 9½ days discharged to take hydrocortisone—100 mg I V every 8 hr for 1 day, prednisone—20 mg daily for 8 days	Recovery

Results of Therapy

Age in Relation to Outcome—Table 2 shows the relation of the age of the patients to the death rate

Table 2—*Mortality in Relation to Age Group in Patients with Pneumococcic Meningitis*

Age Yr	Patients Treated No	Deaths No	Deaths %
0–10	21	4	19
11–20	7	1	14
21–40	12	1	8
>40	15	8	53
Total	55	14	25

The over-all mortality for the 55 cases was approximately 25%, which is essentially the same result obtained during the initial years of penicillin therapy However, it will be noted that there were 21 children 10 years of age and under, the mortality in this group being 19% This favorable outcome is to be compared with results in 15 patients 41 years of age and over, in which the mortality was 53% The grim outlook for patients in the older age group with pneumococcal meningitis and treated with penicillin is comparable to the results of others,[4] in which death rates of up to 80% have been reported

Status of Patient Before Treatment—Besides the age of the patients, there were other factors contributing to a favorable or unfavorable course The duration of illness prior to beginning treatment was definitely related to the outcome The mortality was highest in adults who had been ill for several days, and who had entered in a state of coma The present investigations emphasize the necessity for an early diagnosis of suppurative pneumococcal meningitis, and the prompt institution of intensive antibiotic therapy Other unfavorable factors were debilitating complications such as alcoholism, degenerative diseases, and cirrhosis of the liver

Sequelae of Meningitis—At least 9 of the 41 patients who recovered, or 21%, had serious complications Except for one adult male 30 years of age, all of the sequelae occurred in infants and children under 12 years of age The most common neurological complication involved the cranial nerves, resulting in visual and auditory deterioration Hydrocephalus was observed in two infants A brain abscess was detected in one patient Only a prolonged follow-up period could determine the amount of mental retardment that had occurred as a result of the meningitis

Recurrent Attacks of Pneumococcal Meningitis—There were five patients in this series who had recurrent pneumococcal meningitis The pertinent data for each of these patients are given in table 3 In two patients, (cases 2 and 4, table 3), a demonstrable focus was the cause of the recurrent attacks In case 2, a congenital defect of the dura with fibrosis of the leptomeninges appeared to be causally related to the sixth and fatal attack of meningitis In case 4, chronic otitis media with mastoiditis was the cause of recurrent attacks, and the patient's difficulties were not resolved until a mastoidectomy was carried out

The sequence of events in case 5 was extraordinary The patient, a 39-year-old housewife presented herself at the University Hospitals for the last time with the 15th attack of pneumococcal meningitis As noted in table 3 she had been investigated on two previous occasions at the University Hospitals for pneumococcal meningitis In 1955

TABLE 3—*Recurrent Attacks of Pneumococcic Meningitis in Patients Admitted to University Hospital*

Patient No	Age Yr	Sex	Attacks Prior to Being Seen at University Hospitals	Pertinent Clinical Data on Illness at University Hospitals	Treatment	Outcome
1	40	Male		Admission 1—May 10 1938 semicomatose type 4 pneumococci in CSF	Admission 1—type 4 antipneumococcus rabbit serum sulfanilamide every 6 hr for 7 days	Recovery with bilateral deafness
				Admission 2—May 13 1958 semicomatose pneumococci (type) in CSF	Admission 2—5 million units penicillin I V and I M daily for 15 days 1 Gm sulfadiazine daily for 15 days 100 mg hydrocortisone I V for 7 days	Recovery
2	7½	Male	5 attacks of pneumococcic meningitis associated with congenital defect of dura	Admission 1—Sept 1 1955 6th attack chronically ill lethargic	Admission 1—penicillin 500 000 units every 8 hr tetracycline erythromycin and chloramphenicol for 3 weeks	Died autopsy revealed fibrosis of leptomeninges
3	11	Male	Previous attack in 1944	Admission 1—March 27 1955 2nd attack	Admission 1—penicillin 20 000 units intrathecally 20 000 units I M every 3 hr for 20 days sulfadiazine 1 Gm I V then 2 Gm orally every 4 hr for 1 day	Recovered
4	7	Female		Admission 1—Dec 14 1951 1st attack otitis media	Admission 1—penicillin 1 million units I V every 8 hr for 4 days 200 000 units I M every 6 hr for 16 days Streptomycin 125 mg I M every 6 hr for 11 days chlortetracycline 150 mg I V every 12 hr for 3 days chloramphenicol 250 mg every 6 hr for 7 days Patient told to take penicillin orally at home	
				Admission 2—April 22 1952 2nd attack otitis media	Admission 2—penicillin 1 million units I V daily for 4 days 500 000 units I M every 6 hr for 22 days streptomycin 125 mg every 6 hr for 6 days	Recovered
				Admission 3—Oct 24 1952 3rd attack otitis media pneumococci from CSF	Admission 3—Penicillin 1 million units I V 200 000 units I M every 8 hr for 2 days 1 million units I M every 2 hr for 4 days 500 000 units I M every 8 hr for 6 days 400 000 units I M every 8 hr for 9 days Streptomycin 250 mg every 2 hr for 6 days	Mastoidectomy recovered
5	39	Female	12 attacks of pneumococcic meningitis 1947— 1948—2 attacks 1950—2 attacks 1951—2 attacks 1952—2 attacks 1953— 1954—2 attacks	Admission 1—May 4 1955 13th attack lethargic type 8 pneumococci from CSF and blood	Admission 1—penicillin 1 million units I V every 6 hr for 2 days 600 000 units I M every 6 hr for 11 days 1 million units I V every 12 hr for 9 days Sulfadiazine 4 Gm then 1 Gm every 6 hr for 14 days	Prompt recovery
				Admission 2—May 3 1956 14th attack lethargy type 18 pneumococci from CSF and blood	Admission 2—penicillin 1 million units I M every 6 hr for 5 days 600 000 units I M every 6 hr for 10 days 1 million units I V every 12 hr for 2 days Sulfadiazine 1 Gm every 6 hr for 17 days Discharged on 1 Gm sulfadiazine daily	Prompt recovery
				Admission 3—March 6 1959 15th attack lethargy type 20 pneumococci from CSF and blood	Admission 3—penicillin 3 million units every 6 hr I M for 9 days 4 million units I V every 12 hr for 8 days Hydrocortisone 100 mg I V every 12 hr for 2 days Prednisone 5 mg every 6 hr for 4 days	Prompt recovery left hospital against advice took 500 000 penicillin V orally 4 times daily for 14 days at home

1956, and 1959 she had had recurrent meningitis due to types 8, 18, and 29 pneumococci, respectively. Before being seen at the University Hospitals in 1955 she had been treated for 12 attacks of meningitis. She was thoroughly studied for a primary focus of infection, but none could be demonstrated. No deficiency of the serum proteins was detected. No underlying defection in the immune response was observed, such as is seen in multiple myeloma. Perhaps the patient should have been given antibiotics for a longer period under closer observation, but she was not at all cooperative in this respect.

Comment

Parasitization of the respiratory mucous membrane of the human host by pneumococci still poses a serious medical problem. The magnitude of the problem at Kings County Hospital in Brooklyn has been emphasized by Austrian.[5] He reported that over a period of five years, from 1952 to 1957, 1,354 strains of pneumococci were isolated from 1,322 patients. About two-thirds of the patients had pneumonia. Almost 50% of the patients were harboring types 1 to 8 pneumococci. There were 45 patients per year with pneumococcal bacteremia. Another significant feature of his report was that 180 cases of pneumococcal pneumonia occurred per year on a medical service of 225 beds. During the five-year period, 26 cases of pneumococcal meningitis were treated.

Penicillin has been, and still is, the drug of choice for the treatment of pneumococcal infections. Although penicillin has been widely used in the treatment of a variety of respiratory infections penicillin-resistant strains of pneumococci have not appeared.

Although the fatality rate of pneumococcal meningitis has been reduced significantly, this disease still poses two serious problems. First, the mortality of patients over 40 years of age remains about 50%. Secondly, while the death rate has been lowered for infants and children, the residual damage to the central nervous system is often severe. The vast majority of reports on the treatment of pneumococcal meningitis are concerned with comparative recovery rates. There is an urgent need for long-term follow-up studies on those who have recovered from this illness.

This investigation of 55 patients has emphasized the urgent need for early diagnosis and treatment. Patients whose illness had been prolonged for several days before being seen, or who were comatose when treatment was started, offered the poorest prognosis. Because inflammation of the central nervous system and the leptomeninges does cause severe permanent damage, especially in the form of auditory and visual deterioration, every effort should be made to subdue the inflammation. Besides the prompt use of antibiotics, investigations should be made on anti-inflammatory agents, such as the adrenocortical steroids. Control studies with and without the use of steroids should be carried out, not only in relation to comparable mortality statistics, but follow-up studies on groups should be made with respect to permanent damage resulting from the meningitis.

Summary

From Jan. 1, 1945, to July 1, 1959, 55 bacteriologically proved cases of pneumococcal meningitis were treated at the University of Minnesota Hospitals. There were 14 deaths, giving a mortality of 25%. But eight of the deaths occurred in patients over 40 years of age, and in this group the death rate was 53%.

The most common primary focus of infection was otitis media, occurring in 18 patients, or 32.7%. Pneumonia was present in only 4 of the 55 patients.

In treating pneumococcal meningitis, penicillin is the drug of choice. The antibiotic should be given intravenously in a dose of 1 million units per hour until definite improvement occurs, then 4 to 5 million units administered intramuscularly every 6 hours. Penicillin should be given for at least two, and preferably three weeks. Intrathecal administration of penicillin is not recommended. It is suggested that sulfadiazine be given orally as long as penicillin is administered.

Other supportive measures include eradication of the primary focus, such as mastoidectomy, which was carried out in three cases. Further investigations should be made on the use of adrenocortical steroids in conjunction with penicillin.

Attention is called to the serious sequelae of pneumococcal meningitis in those patients that recovered, especially in infants and in children. There were five patients with recurrent attacks of pneumococcal meningitis, one patient having had 15 different attacks.

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HYPOTENSIVE EFFECTS OF IPRONIAZID AND CARBOXAZID

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The authors have investigated the hemodynamic changes accompanying the hypotension that occasionally follows administration of amine oxidase inhibitors, particularly iproniazid phosphate Iproniazid was given intravenously and orally, in varying doses, to hospitalized patients with toxemia of pregnancy or with essential hypertension associated with pregnancy Similar observations were made with carboxazid, an analogue of iproniazid Data on blood pressure in supine and upright positions and on renal hemodynamics and cardiac output indicated that the hypotension was probably caused by venous pooling and by a decrease in the cardiac output rather than by a true vasodilator action

Several investigators have observed a certain degree of hypotension after the administration of amine oxidase inhibitors, particularly iproniazid (Marsilid) phosphate[1] Others attempting to evaluate this action in ambulatory hypertensive patients have found that daily doses of 100 to 600 mg of this drug produced orthostatic hypotension which varied in degree from patient to patient[2]

The present study was aimed at investigating the hemodynamic and renal effects of acute and chronic administration of iproniazid in patients with (1) toxemia of pregnancy and (2) essential hypertension associated with pregnancy Similar observations on the effects of carboxazid (Marplan), a newly developed analogue of iproniazid, have also been included

Material and Methods

The study was divided into four parts, and the methods and the materials used for each part are described

Part 1—Iproniazid was administered intravenously to 15 hospitalized patients (10 with toxemia of pregnancy and 5 with essential hypertension associated with pregnancy) The criteria for the diagnosis of toxemia of pregnancy have been outlined elsewhere[3] The patients were given bed rest for 10 to 24 hours prior to the test Control blood pressure recordings (by Sphygmomanometer) were taken every 1 to 2 minutes for 30 to 40 minutes prior to injection of the drug Thereafter, iproniazid was given in rapid intravenous injections in doses varying from 0 7 to 2 mg per kilogram of body weight Blood pressure and pulse rate continued to be recorded every minute for about 30 minutes, with the patient in the supine position, and for another 20 to 30 minutes, with the patient in the standing position Further recordings were taken when the patient resumed the recumbent position

Part 2—Iproniazid was administered orally to 12 untreated, hospitalized patients (5 patients with toxemia of pregnancy and 7 with essential hypertension) In each patient, control blood pressure readings were recorded four times daily for two to four days Thereafter, iproniazid was given orally in progressively increasing doses from 50 mg to 150 mg per day During the treatment, four to six blood pressure recordings were taken daily, with the patient in the recumbent position Ten to 12 blood pressure recordings were taken daily, with the patient in a standing position

Part 3—The effect of iproniazid-induced hypotension on renal hemodynamics and cardiac output was investigated in four patients with essential hypertension associated with pregnancy Renal blood flow and glomerular filtration rate were measured by the para-aminohippurate and inulin clearances according to techniques described elsewhere[3] Renal vascular resistance was estimated from the arterial blood pressure and renal blood flow Cardiac output was determined by the conventional dye technique Control values were obtained when the patients were given iproniazid therapy, but they had shown no hypotensive effect The same studies were repeated during the hypotensive phase and when the drug was either withdrawn or the dose reduced and blood pressure had returned to control values (normal)

Part 4—The effects of orally administered carboxazid on blood pressure and renal hemodynamics were studied in patients with essential hypertension associated with pregnancy The procedure was similar to that described in Part 3 except that carboxazid (instead of iproniazid) was given, in doses of 10 to 20 mgs per day

Results

The results of the four parts of the study are presented in corresponding sequence

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Effects of Intravenous Administration.—Figure 1 shows a typical response to iproniazid in a patient with severe preeclampsia, whereas Figure 2 illustrates a typical response of a patient with essential hypertension. The other patients responded in a similar manner. It is evident that iproniazid in the doses given had no significant effect on the patient's blood pressure with the patient in either the supine or the upright position. The patient's pulse rate, likewise, did not change. When ipronoazid was given at high doses, bizarre side-effects such as flushing, dizziness, and mental stimulation were observed.

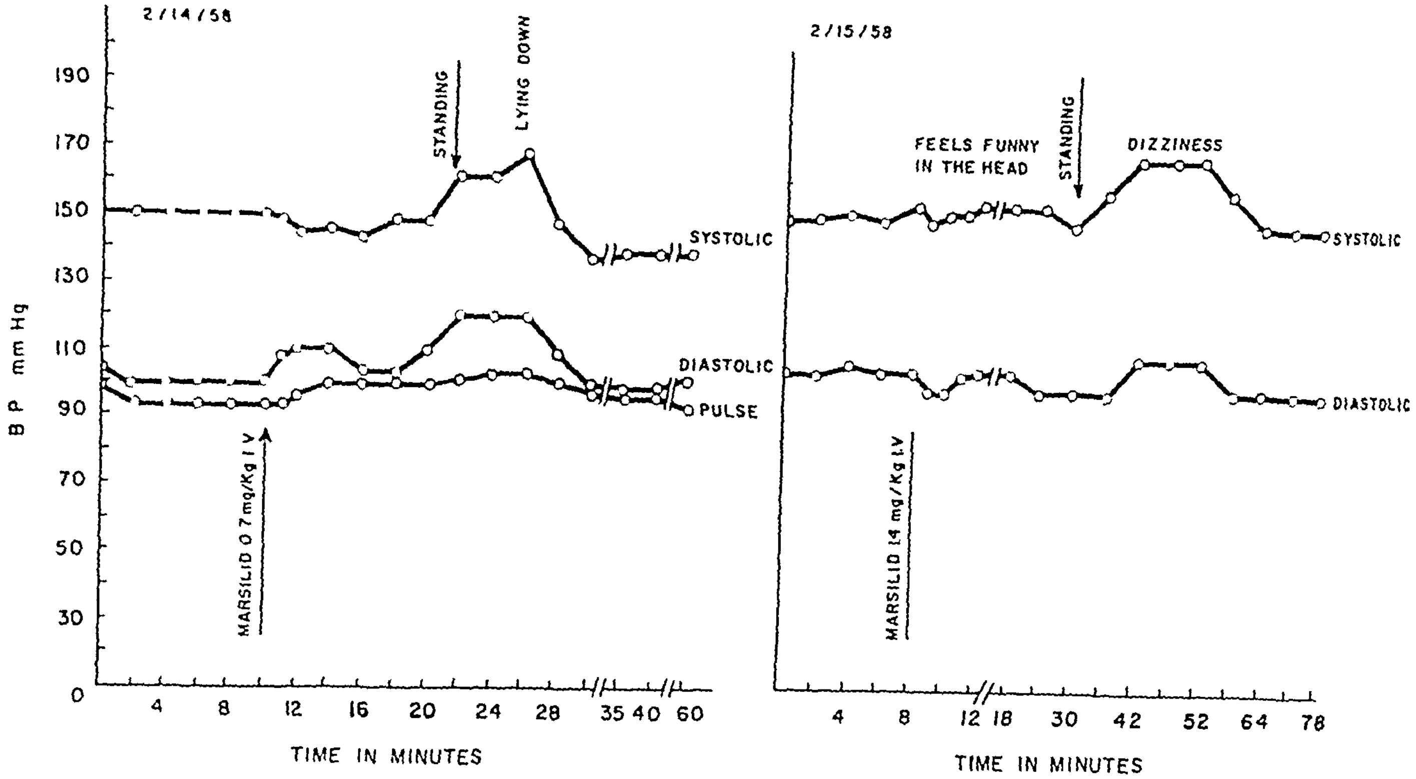

Fig. 1.—Effects of intravenous administration of iproniazid (Marsilid) phosphate on blood pressure and pulse rate of a pregnant patient with preeclampsia. In the first test, 0.7 mg. per kilogram of body weight was given, with lack of postural hypotensive effect. Twenty-four hours later, 1.4 mg./kg. was given without hypotensive action.

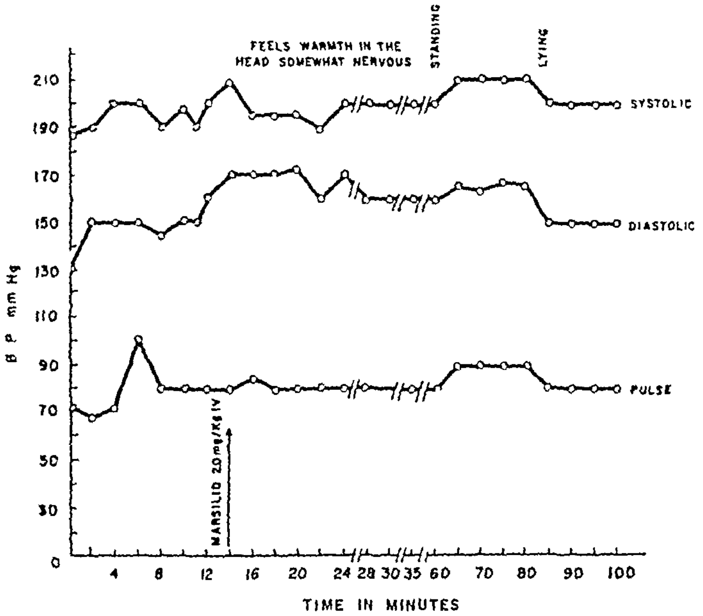

Fig. 2.—Effects of intravenous administration of 2.0 mg./kg. of iproniazid (Marsilid) phosphate to patient with essential hypertension. Despite appearance of side-effects, no hypotensive action was observed.

Effects of Oral Administration of Iproniazid.—The results of orally administered iproniazid varied according to the dose and varied with the same dose in different patients. Figure 3 illustrates the response of a patient with essential hypertension, whereas table 1 summarizes all the data. No postural hypotension was observed during the administration of 50 mg. of iproniazid per day. However, when the dose reached 100 to 150 mg. per day, a moderate to severe orthostatic hypotension occurred and became evident approximately 30 to 40 minutes after ingestion of the drug. The patient felt a sensation of fainting and imminent collapse which was accompanied by a blood pressure fall that varied from 30 to 40 mm. Hg systolic and 10 to 30 mm. Hg diastolic. The patient's blood pressure and general condition improved when she re-assumed a supine position. It is of interest that some patients with the same degree of hypertension, who received the same dose of iproniazid, did not have a postural effect. Again, at high doses, the drug induced some bizzarre mental side-effects, which, in many instances, could not be accurately described.

Effects of Iproniazid on Renal Hemodynamics and Cardiac Output.—Table 2 lists the values for renal hemodynamics and cardiac output during the periods of control, iproniazid-induced hypotension and recovery. A marked decrease in urine flow, renal plasma flow, glomerular filtration rate, and cardiac output occurred when the blood pressure fell, and vascular resistance increased. When hypotension subsided with the patient's resumption of the recumbent position, the values for renal hemodynamics and cardiac output returned to control levels

Effects of Carboxazid—In the doses given, carboxazid had no significant action on the supine blood pressure and on the renal plasma flow and glomerular filtration rate Control blood pressure ranged from 160/95 mm Hg to 210/120 mm Hg It remained practically the same after administration of carboxazid Postural hypotension occurred in three cases, but in only one case was it severe enough to warrant discontinuance of therapy

Comment

It is evident from the present data that the fall in blood pressure which follows the administration of iproniazid and its analogue, carboxazid, is inconsistent and requires continuous oral administration of 100 to 150 mg per day of iproniazid or 20 mg or more of carboxazid for a few days to become evident Given intravenously in doses up to 2 mg per kilogram of body weight, iproniazid failed to produce any hypotensive action Thus, the occurrence of hypotension seems to depend upon the establishment of a critical blood level through cumulation However, since not all patients exhibit the same vascular response, it seems also that the hypotensive action of iproniazid and its analogue is peculiar to certain subjects

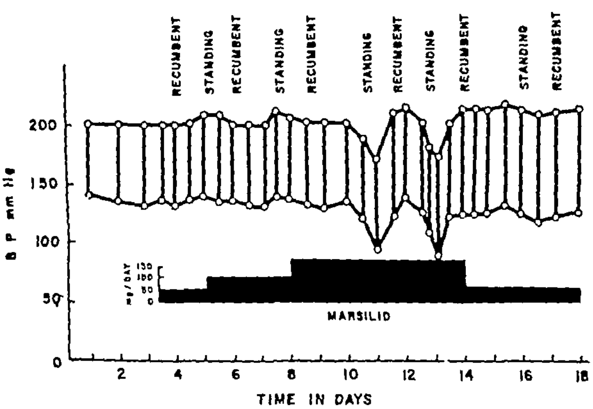

Fig 3 —Effects of oral administration of iproniazid (Marsilid) phosphate to hospitalized patient with essential hypertension in whom orthostatic hypotension occurred When dosage reached 150 mg/day for 3 to 4 days, postural hypotension of varying magnitude began to occur one half hour after ingestion of drug Patient's hypotension was relieved rapidly by reassuming recumbent position When dose was decreased, orthostatic effect subsided

As to the hemodynamic mechanisms of this hypotension, the present data seem to indicate that it is orthostatic in nature, probably caused by venous pooling This hypothesis receives support from the clinical observations[4] which indicate that the fall in blood pressure is more evident when the patient assumes the upright position This fact together with the striking decrease in cardiac output, renal plasma flow, and glomerular filtration rate, as well as the increase in renal vascular resistance, simulate the hemodynamic action of ganglionic blocking agents[5] Whether iproniazid in large doses produces, by some unknown mechanism, a blockade of the venomotor tone and a sequestration of blood into the venous side of the circulation cannot be stated from the present study

Table 1 —*Effects of Oral Administration of Iproniazid on Patients' Blood Pressure as Compared with Control Blood Pressure*

		Test Results				
		Daily Dose mg	Length of Treatment Days	Supine Blood Pressure		Postural Hypotension
Diagnosis	Patient			C*	A†	
Toxemia	1	50	3	160/110	150/105	0
		100	3	150/104	150/100	0
	2	50	4	170/112	172/114	0
		150	2	170/110	162/110	moderate
	3	50	3	150/90	148/88	0
		150	3	150/88	142/88	0
	4	100	3	165/108	160/110	moderate
		150	3	160/110	155/100	severe
	5	50	4	180/108	175/104	0
		150	2	175/105	170/100	moderate
	6	50	6	190/110	180/100	0
		150	5	180/100	180/104	severe
Essential Hypertension	7	100	8	180/110	175/100	severe
	8	50	2	200/140	200/140	0
		100	3	210/145	200/140	0
		150	6	204/150	210/160	severe
	9	150	6	170/110	170/112	0
	10	50	5	190/105	200/110	0
		150	3	200/110	180/105	moderate
	11	100	12	160/95	170/110	0
	12	50	4	185/105	190/110	0
		100	3	190/110	175/105	0
		150	3	175/105	180/110	severe

* C control blood pressure represents average of all the readings recorded prior to drug administration

† A, response to drug, as tabulated for each patient according to the dose given and refers to the lowest readings recorded during therapy

From the clinical point of view, it seems unlikely that the hypotension induced by use of iproniazid is of any benefit to the hypertensive patient Its inconsistency together with the unfavorable hemodynamic and renal effects indicate that the fall in blood pressure is a side-effect rather than a true vasodilator action

Table 2 —*Effects of Iproniazid Therapy During Control, Hypotension, and Recovery Periods*

		Test Results*				
Patient	Period	UF ml/min	RPF ml/min	GFR ml/min	RV mm Hg/ml/min	CO Liter/min
	Control	4 8	[illegible]	115	7	5 6
1	Hypotension	1 1	380	85	14	4 1
	Recovery	2 8	485	98	8	[illegible] 2
	Control	3 7	615	125	10	
2	Hypotension	0 8	425	75	[illegible]	
	Recovery	4 1	535	110	12	
	Control	2 9	515	108	6	7 2
3	Hypotension	0 7	465	70	12	4 8
	Recovery	3 1	[illegible]	110	7	6 9
	Control	5	[illegible]	128	[illegible]	
4	Hypotension	1 0	495	101	13	
	Recovery	4 2	610	135	6	

* UF urine flow RPF renal plasma flow GFR glomerular filtration rate RV renal vascular resistance CO cardiac output

Summary and Conclusions

The hemodynamic and renal effects of acute and chronic administration of Marsilid and its analogue, Marplan, were investigated in patients with toxemia of pregnancy and in patients with essential hypertension associated with pregnancy Acute intravenous injections of iproniazid in doses varying between 0 7 mg and 2 0 mg per kilogram of body weight did not produce any hypotensive effect with the patient in either a supine or a standing position Oral administration of iproniazid in doses of 100 to 150 mg per day elicited orthostatic hypotension in about 50 per cent of the cases This hypotension was accompanied by a decrease in cardiac output, urine flow, renal plasma flow, and glomerular filtration rate Renal vascular resistance increased Oral administration of carboxazid in doses of 10 to 20 mg produced inconsistent orthostatic hypotension

On the basis of the present data, it is concluded that the hypotension associated with the use of iproniazid or with the use of its analogue, carboxazid, represents a side-effect rather than a true vasodilator action It is probably caused by venous pooling and a decrease in the cardiac output

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The iproniazid and carboxazid used in this study were provided as Marsilid and Marplan, respectively, by Hoffmann La Roche, Inc , Nutley, N J

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HYDRAMNIOS AND CONGENITAL ANOMALIES

STUDY OF SERIES OF SEVENTY-FOUR PATIENTS

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A series of 74 patients with hydramnios was studied, 80% were multiparas and there were five sets of twins There was a high rate of cesarean section (21 6%), breech deliveries (6 8%), diabetes (18 9%) and preeclampsia (14 9%) Among the 79 neonates delivered, there were 23 deaths and the perinatal mortality was 29 1% There is a remarkable association of hydramnios and congenital anomalies, 21 infants (26 6%) had congenital anomalies and 14 (17 7%) had pathological conditions Anencephaly and hydrocephaly were the most common lesions, 6 infants had gastrointestinal defects and 10 had anomalous lesions which would have obstructed swallowing or prevented the passage of fluid through the gastrointestinal tract while in utero Special emphasis should be placed on lesions in which there is urgent need for correction of respiratory obstruction, early surgery, or both Routine gastric catheterization and aspiration are therefore valuable diagnostic procedures

Hydramnios has been associated with a high incidence of congenital anomalies and mortality in infants for many years (table 1) Recently this relationship has been suggested as a diagnostic sign in early recognition and guidance to the therapy of obstruction in the alimentary tract of the newborn infant[1]

The purpose of this report is to present our experience with this disorder from 1953 to 1958 at the Sloane Hospital for Women and to emphasize a method of diagnosis which is used at this hospital to facilitate the discovery of gastrointestinal obstruction in all infants In addition, the physiological processes involved in the normal and pathological formation of amniotic fluid are reviewed

In data compilation, both mother and infant clinical records were used Only those cases were accepted in which there was convincing clinical evidence of excessive accumulation of amniotic fluid Two liters were taken as the upper limit of normal[2] The cases of acute and chronic hydramnios were analyzed together

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History

Incidence—Collecting the amniotic fluid is difficult and uncertain and the resultant diagnosis is usually made solely on clinical impression In milder cases of hydramnios the frequency of recognition will vary with the individual observer For this reason the incidence of hydramnios varies greatly with different reports and ranges from 1 case in 62 deliveries[3] to 1 case in 754 deliveries[4] as shown in table 1 In 24,316 deliveries at the Sloane Hospital during the years 1953 to 1958 there were 74 cases of hydramnios, an incidence of 1 case in 329 deliveries This frequency agrees closely with the statistics of the Johns Hopkins Hospital as reported by Eastman[2] The combined figures of Ryder[5] in 1932, Yordan and D'Esopo[6] in 1955, and the present study total 78,616 deliveries at the Sloane Hospital for Women, with 391 cases of hydramnios, a frequency of 1 case in 201 deliveries

TABLE 1—*Perinatal Mortality and Congenital Anomalies Associated with Hydramnios*

Author	Cases No	Incidence*	Infants No	Perinatal Mortality %†	Congenital Anomalies %‡
Poeck[18] 1923	103		136	60	12 5
Floris[10] 1923	224		256	29	9 0
Taussig[7] 1927	32	1 200	35	44	20 0
Ryder[5] 1932	113	1 177	129	50	4 0
Mueller[4] 1948	66	1 754	70	56	29 0
Macaffee[12] 1950	147	1 82	172	56	46 0
Prindle[8a] 1955	146	1 278	155	51	44 0
Yordan and D'Esopo[6] 1955	204	1 168	219	44	30 0
Eastman[2] 1956	178	1 358	200	48	15 5
Scott and Wilson[1b] 1957	169	1 166			29 5‡
Lloyd and Clatworthy[1a] 1958	76	1 232	76		16 0
Barry[3] 1958	213	1 62	231	69	59 5
Present study	74	1 329	79	29 1	26 6
Average		1 373		48 7	26 7

* Based on total number of deliveries
† Based on total number of infants
‡ Congenital anomalies associated with interference with fetal alimentation

Parity, Multiple Births, and Type of Delivery—Eighty per cent of the 74 mothers were multiparas A similar high incidence of multiparous patients was also reported by Taussig[7] in 1927 There were five sets of twins in the series, representing 6 8% of the cases This is seven times the usual occurrence of twins in the general patient population of Sloane Hospital during this period With the exception of Lloyd and Clatworthy,[1a] the high frequency of multiple pregnancies is apparent in all reported groups of cases

The types of delivery were interesting because the rates of cesarean sections (21 6%) and breech deliveries (6 8%) were significantly higher than the usual incidences of 8 5% and 3 4% respectively The high cesarean section rate reflects the large number of diabetic patients found in the series (table 2)

Associated Complications of Pregnancy—Table 2 lists the associated complications of pregnancy found in the series The 18 9% incidence of diabetes is striking when compared to the average frequency of 0 42% at this hospital It will be noted that the incidence of preeclampsia is 14 9% This is about three times the expected rate in our patient population There were five patients with Rh incompatibility as evidenced by elevated agglutinin titers, erythroblastotic infants, or both The frequent association of hydramnios with diabetes, toxemia and Rh incompatibility is well-recognized[8] but its relative significance to the pathological accumulation of amniotic fluid is speculative Plentl[9] believes that the common denominator is a metabolic or mechanical placental pathological change which may embarrass the placental-fetal circulation

Fetal Outcome—Seventy-nine babies were delivered from the 74 patients in this series There were 23 fetal deaths, including 16 stillbirths and 7 neonatal deaths, the over-all perinatal mortality was 29 1% This percentage represents one of the lowest perinatal loss rates reported for this syndrome (table 1) Floris[10] in 1923 had an almost identical incidence, but he was dealing with a large number of mild cases The reason for this low rate is not apparent from the analyzed data Eleven infants of this group had congenital anomalies, 10 infants had pathological abnormalities, and 2 infants were premature

TABLE 2—*Associated Complications of Pregnancy in Seventy-four Patients**

Complications	Patients No	Patients %	Total Incidence at Hospital %
Diabetes mellitus	14	18 9	0 42
Preeclampsia	11	14 9	4.5
Hypertensive vascular disease	2	2 7	1 6
Heart disease	2	2 7	1 5
Rh incompatibility	5	6 8	
Psychiatric disease	4	5 4	
Fibromyomas of uterus	2	2 7	
Epilepsy	2	2 7	
Anemia	2	2 7	
Thyrotoxicosis	1	1 4	
Late latent lues	1	1 4	
Hypothyroidism	1	1 4	
Intercapillary glomerulosclerosis	1	1 4	
Kyphoscoliosis with atelectasis	1	1 4	
Pyelonephritis	1	1 4	
Hyperemesis gravidarum	1	1 4	
Mucous colitis	1	1 4	
Adrenal cortical hypofunction	1	1 4	
Total	53		

*In 43 of these patients history laboratory findings and results were normal

Forty-one of the infants (51 9%) were apparently normal, and all survived There was a high total frequency (19%) of prematurity which is consistent with the reports of others[6] This is two and one-half times the usual incidence at Sloane Hospital Only 3 of the 15 premature infants had no other associated abnormality One of these was a 250-Gm nonviable fetus

Congenital anomalies were present in 21 babies These include anencephaly, hydrocephaly, microcephaly, spina bifida, mongol, volvulus, tracheoesophageal fistula with atresia esophagus, imperforate anus, cleft palate, congenital heart disease, pyloric stenosis, genitourinary disease, deformed extremities and agenesis of ears Pathological conditions were found in 14 other infants These include maceration, erythroblastosis, tight nuchal cord, hyaline membrane disease, edematous (diabetes) and meconium aspiration. Multiple anomalies were found in eight infants. Anencephaly was the most common lesion, but its incidence did not approach Barry's[7] 38.1% or Prindle's[8a] 23.4%. Hydrocephaly was the next most frequent type of anomaly. There were six babies with gastrointestinal defects, including three cases of volvulus, of which one was due to an atresia of the upper jejunum. Interestingly enough, one case of pyloric stenosis was diagnosed and an operation was performed when the infant was eight weeks of age. This may represent a coincidental finding. Altogether, an incidence of 13.5%, 10 infants had anomalous lesions which would either prevent swallowing or obstruct the passage of fluid through the gastrointestinal tract while in utero. Scott and Wilson,[16] on the other hand, found this to be true in 29.5% of their cases.

TABLE 3.—*Pathological Abnormalities Associated with Hydramnios*

Type	Live Births	Stillbirths and Neonatal Deaths	Total
Maceration		6	6
Erythroblastosis	2	1	3
Tight nuchal cord	1		1
Hyaline membrane disease		2	2
Edematous (diabetes)	1		1
Meconium aspiration		1	1

Physiology of Amniotic Fluid

Many theories to explain the formation of amniotic fluids have been proposed, however, only three have received serious consideration. A fourth theory would consider the fluid of mixed origin. The oldest and simplest explanation is to regard this fluid as a product of fetal urination. It is true that the fetal kidney excretes urine in utero, however, this probably represents only a very small portion of the total amount of fluid present.[11]

Another possible source of the fluid is the amniotic epithelium which has been shown to have secretory characteristics. Although the organic constituents of the amniotic fluid may be derived in this manner, the water itself must come from some more effective source in order to be produced in such large quantity.[9] The third possible source is transudation from the maternal blood, the amnion regulating the passage of fluid in a manner similar to that of the peritoneum and pleura which results in a dialysate or ultrafiltrate of plasma. However, recent experimental work cannot substantiate this theory.[9]

The amniotic fluid is not a stagnant pool. On the contrary, there is experimental evidence that the exchange of the water content is a rapid process. Vosburgh and others[12] injected deuterium oxide (heavy water) into a maternal vein, and by sampling the amniotic fluid for the appearance of the isotope, found that, on the average, 35.4% of the water of the amniotic fluid is replaced every hour by water from the maternal plasma. This finding indicates that the entire water content changes about every three (2 hrs 54 min) hours. Investigation by Plentl and his group,[9] with isotopic tracers, led to a quantitative formulation of the over-all exchange between mother, fetus, and amniotic fluid. They found a net circulation of 600 ml per hr from mother to fetus to amniotic fluid and back to mother. In this circulation the water and electrolytic constituents are exchanged at their own individual rates and not en bloc. The amniotic fluid, therefore, cannot be a transudate or a dialysate of maternal plasma. However, these experiments do not give specific information on the site of exchange but only describe its over-all mechanism of exchange.

The removal of the amniotic fluid is enveloped in as much speculation as its formation. There may be transudation from amniotic fluid to mother by way of the amnion, decidua, and placenta, or the fetus may swallow or inhale it.[9] Macaffee[13] believed that the only area capable of exchanging adequate amounts of fluid is the fetal lung. The evidence for this is the finding of lanugo hair in fetal alveoli at autopsy and the demonstration of fetal respiratory movements in utero. However, James,[14] in a recent review of this subject, concluded that the lungs may be a source of fluid rather than a site of absorption and that respiratory movements, being stimulated by asphyxia, only occur abnormally in the later period of gestation.

TABLE 4.—*Congenital Anomalies Associated with Hydramnios*

Type	Live Births	Stillbirths and Neonatal Deaths	Total
Anencephaly		5	5*
Hydrocephaly	1	3	4
Microcephaly		1	1
Spina bifida	1		1
Mongol	1		1
Volvulus			3*
With atresia upper jejunum	1		
With congenital bands of upper jejunum		1	
With common mesentery and herniation of liver		1	
Tracheoesophageal fistula with atresia esophagus	1	1	2*
Imperforate anus		1	1
Cleft palate	1	1	2
Congenital heart disease	2	1	3
Pyloric stenosis	1		1
Genitourinary disease	3	2	5
Deformed extremities		1	1
Agenesis of ears		1	1

*Congenital anomalies definitely associated with interference with fetal alimentation in utero

The simplest removal of this fluid would be via absorption through the fetal alimentary tract and then return to the maternal circulation via the placenta. That the fetus swallows amniotic fluid is a well-established fact.[15] Plentl and Gray[9] on the basis of in vivo experiments and hydrodynamic models concluded that at least 25%, and probably more than 50%, of the water transfer from the amniotic fluid to mother is through the fetus as intermedium. To what extent this is accomplished by fetal deglutition is unknown.

Etiology of Hydramnios

The most obvious explanation for hydramnios is that it is produced by either an overproduction or a deficient removal of amniotic fluid. The transfer of water is of such magnitude that a small difference of only a few milliliters per hour in the exchange rate could result in the clinical syndrome of hydramnios.

The close association of hydramnios with congenital anomalies (table 1), particularly those anomalies in which there is some interference with fetal deglutition or alimentation,[15] indicates a causal relationship. This leads to the hypothesis that a failure of the fetus to remove amniotic fluid, due to an obstruction of the passage of fluids in the proximal portion of the gastrointestinal tract (e.g., esophageal or duodenal atresia) or inability to swallow (e.g., anencephaly), would result in an excessive accumulation of liquid. Anencephaly may also be associated with an increased transudation of fluid from the exposed meninges into the amniotic cavity.[7] On the other hand, this syndrome may not be found if there is only a partial anencephaly with a medulla present. This would allow swallowing to take place. The occurrence of an obstructive lesion which does not result in hydramnios may be due to its distal location permitting proximal absorption (e.g., ileal atresia, meconium ileus or imperforate anus). In addition, there may be an incomplete obstruction, a wide tracheoesophageal fistula (type C) or the rare type of esophageal atresia (type D) in which both segments of the esophagus communicate with the trachea, thereby providing a route by which the fluid can reach the lower gastrointestinal tract.[3] However, this simple and convenient theory does not account for the occurrence of this syndrome in the presence of congenital anomalies in which the passage of fluid is not blocked or in the large proportion of completely normal infants.

Plentl,[8] on the basis of his physicochemical investigations on water exchange, implicates the fetal circulation and placenta as being etiological factors. This could account for the frequent association of this entity with such maternal diseases as toxemia, diabetes, and Rh incompatibility, all of which are characterized by abnormal placentae.

With the dynamic exchange of fluid perhaps we are dealing with multiple sites for interference, any one or a combination of which could produce an imbalance of only a few milliliters per hour in the transfer rates, which would result in the syndrome of hydramnios.

Diagnosis of Delivery Room Anomalies

Regardless of the precise pathophysiological mechanism involved, the remarkable association of hydramnios with congenital anomalies cannot be denied. Twenty-seven per cent of all the infants reported on in the literature had anomalies (table 1). Special emphasis should be placed on those lesions in which there is urgent need for correction of respiratory obstruction, early surgical therapy, or both.

Since it is particularly true of the obstructive gastrointestinal lesions that the longer the condition goes unrecognized the worse the prognosis becomes, it would behoove us to study and make a definite diagnosis in these infants as soon as possible. Recently it has been recommended[1] that in order to avoid a delay in diagnosis a catheter should be passed into the stomach of the infant to demonstrate the continuity of the esophagus. In addition, a small amount of air can be injected, thereby providing a contrast medium for roentgenographic evidence of other obstructive lesions within three hours of birth.[1a]

In 1949, Gellis, White, and Pfeffer[16] first directed attention to the large volume of gastric contents found in infants delivered by cesarean section of diabetic mothers. They proposed routine gastric suction in these infants as a prophylactic measure against future regurgitation and aspiration. Since 1952 it has been the policy at the Sloane Hospital for Women to catheterize and aspirate the stomach of every infant without regard to the route of delivery. This is performed as soon as the respirations of the infants are well established. A soft two-holed no. 12 Rusch rubber catheter is attached to a glass bulb (De Lee) with a one-way trap and a rubber suction mouth piece. If the tip of the catheter is not seen in the left half of the abdomen, a stethoscope is placed over the abdomen and a short puff of air is used to confirm its position. There is a threefold purpose for this routine catheterization. The first purpose, the possible prevention of regurgitation and aspiration, has been mentioned. However, perhaps the more important reasons are the ruling out of the presence of esophageal atresia and the measuring of the gastric contents. The average volume found in infants delivered by cesarean section is 7.2 cc (range 0 to 50 cc), in breech deliveries it is 4.3 cc (range 0 to 15 cc), and in vaginal vertex it is 5.7 cc (range 1 to 20 cc). If 25 to 50 cc are aspirated, an obstructive lesion of the upper gastrointestinal tract should be suspected and the infant studied closely with flat plates of the abdomen, further emptying and measuring of stomach contents, meanwhile withholding fluids by mouth. However, if over 50 cc are aspirated initially, x-rays are taken within the hour. The absence of gas below the pylorus indicates obstruction and necessitates early exploration.

During the time that this routine has been used, six infants born at Sloane Hospital were found to have intestinal obstruction during the neonatal period (table 5). Four of the six babies had 38 cc or more fluid present on gastric aspiration while still in the delivery room. Of the two with small quantities of fluid, the one in case 6 may have had volvulus developing sometime after birth, since the child was well for the first 10 days of life. From these data it would appear that through the simple technique of measuring the gastric contents immediately after delivery, 80% of the in utero intestinal obstructions may be diagnosed

Routine catheterization has not been as successful in the early diagnosis of tracheo-esophageal fistula with esophageal atresia In only two of five infants born with this condition in the six-year period was the condition discovered in the delivery room This may represent errors in technique on the part of inexperienced personnel This is well illustrated by a case of atresia that was missed by four separate people using as the only criterion of patency the depth to which the catheter entered the esophagus The position of the catheter and the diagnosis were later confirmed by gently puffing down the tube

Freeman and Scott[17] believe that leaving the stomach empty has a favorable effect in the prevention of regurgitation and aspiration, with the subsequent development of pulmonary complications No such relationship has yet been found at this clinic

TABLE 5—*Results of Gastric Aspiration in Infants Born at Sloane Hospital, Between Late 1952 and 1958, with Intestinal Obstruction During the Neonatal Period*

Case No	Pathology	Hydramnios	Fluid by Gastric Aspiration Cc *	Operation	Outcome
1	Congenital bands of upper jejunum, with volvulus	present	50	Lysis of adhesions enteroenterostomy	*Died 13 hours after birth*
2	Atresia of upper jejunum	present	50	Gastrojejunostomy 3 days after birth	*Died 7 days post operatively*
3	Atresia of upper jejunum with volvulus	present	75	Operated on 3rd day after birth	Recovered
4	Partial atresia of 2nd part of duodenum	absent	38	Jejunoduodenostomy 2nd day after birth	Died 8 days post operatively
5	Volvulus with common mesentery and herniation of liver and multiple congenital anomalies	present	3	Ileostomy 1 day after birth	Died 2 days post operatively
6	Volvulus with malrotation of intestines	absent	†	Operated on twice for recurrent volvulus (21st and 29th day)	Died 25 days post operatively

* Aspiration performed in delivery room
† Small amount of meconium removed

Summary

Seventy-four cases of hydramnios occurring at the Sloane Hospital for Women in the years from 1953 to 1958 were analyzed with reference to parity, twin births, type of delivery, complications of pregnancy, and fetal outcome There was a significantly higher incidence of multiparas, twin pregnancies, cesarean sections, and breech deliveries in mothers with hydramnios than in the general patient population The incidence of diabetes mellitus (19%) and preeclampsia (15%) was remarkably greater than the usual rates of 0 42% and 4 5% respectively Forty-one of the 79 infants were apparently normal, and all survived Congenital anomalies were present in 21 (26 6%) and pathological abnormalities in 14 (17 7%) The over-all perinatal mortality was 29% A technique of routine gastric catheterization and aspiration for all infants was used as a method of diagnosis of congenital anomalies of the upper gastrointestinal tract

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MAINTENANCE OF RESPIRATION IN THE NEONATAL RESPIRATORY DISTRESS SYNDROME

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Management of a case of severe respiratory distress syndrome in a newborn boy consisted of endotracheal intubation and maintenance of respiration with a mechanical ventilator for four days Roentgenograms gave evidence of progressive clearing of the lungs during this time Physical exhaustion contributes significantly to respiratory failure in infants with this syndrome Most infants weather the period of respiratory distress and recover without sequelae, but in those who die the clinical picture is one of progressive dyspnea, increased efforts to breathe, exhaustion, and death from anoxia Prolonged application of artificial ventilation to infants with severe distress may prevent exhaustion

In 1958 Benson and others [1] reported the successful management of three cases of severe pulmonary insufficiency in the newborn infant by the employment of positive pressure ventilation with a respirator by means of tracheostomy The efficacy of prolonged positive pressure ventilation in treating acute respiratory insufficiency in adults has long been realized [2], however, we have been unable to find any other reports of its use in respiratory problems of the newborn The successful prevention of what appeared to be an inevitable death from respiratory distress prompted us to submit the following case report

Report of a Case

A 2,480-Gm (5 lb) male infant, born after an uneventful spontaneous delivery with an Apgar rating of 9, did well for one hour Subsequently substernal retraction, tachypnea, and cyanosis occurred and respiratory failure rapidly ensued Tracheal intubation was accomplished with a no 14 Portex tube and artificial ventilation started with a bag and mask The trachea at the time was seen to be clear, and a roentgenogram taken a few minutes later revealed a marked generalized increase in pulmonary density and a well-outlined bronchial tree, as in the hyaline membrane syndrome (see figure) [3] Assisted respirations were necessary since the infant, if allowed to breathe alone, continued with shallow and ineffective respirations After 12 hours of intermittent bag breathing, the infant was still unable to sustain his own respirations and it was decided to employ an automatic respirator The Stephenson respirator was selected since it is a volume-limited, pressure-variable unit which can achieve a rapid respiratory rate [4] A metal Ayre's T-piece was connected directly to the endotracheal tube and to the respirator by means of stiff rubber tubing with an internal diameter of 0 5 in A humidified mixture of oxygen and compressed air flowing at 6 liters per minute entered at the side arm of the T-piece, and, since the flow was several times the estimated minute volume, the system functioned on the Ayre's principle [5] The pressure limiting control was set at its maximum point, 30 mm Hg (40 8 cm H_2O), and then the volume control was adjusted until the point was reached where adequate ventilation, as determined by chest expansion and auscultation, was achieved Respiratory rate was set at about 48 per minute

Improvement in general condition began as soon as respirator therapy was started The infant did not become apneic until 12 hours later in spite of seemingly adequate expansion of the chest by the respirator When apnea was finally induced, the results were most gratifying, the infant slept or sucked contentedly on the endotracheal tube

Forty-eight hours after birth, artificial ventilation was stopped because of the improvement in the infant's condition After one hour of spontaneous respirations, the endotracheal tube was removed Initially the infant did well, but progressive retraction recurred and two hours later the infant quickly tired, respirations slowed and stopped, and the heart rate fell to 40 per minute Immediate reintubation was accomplished At first, considerable positive pressure was necessary to reinflate the lungs Indeed, a pressure greater than the limit of the respirator (30 mm Hg) was necessary This was accomplished by puffing directly into the endotracheal tube in a manner similar to that in which smoke rings are blown This allowed volume control and short-lived pressure peaks As Goddard has demonstrated clinically, positive pressures of 30 to 60 cm H_2O applied over a 0 2-second interval may be employed to correct atelectasis, but pressure should be reduced soon thereafter [6] Machine cycled respirations were then resumed, and the infant was maintained for another two days on the respirator until dried mucus blocking the lumen of the endotracheal tube necessitated unscheduled removal of the tube After extubation some retraction was noted, but because of the apparent lack of dyspnea it was elected to observe the infant As Benson also noted, after respirator therapy some

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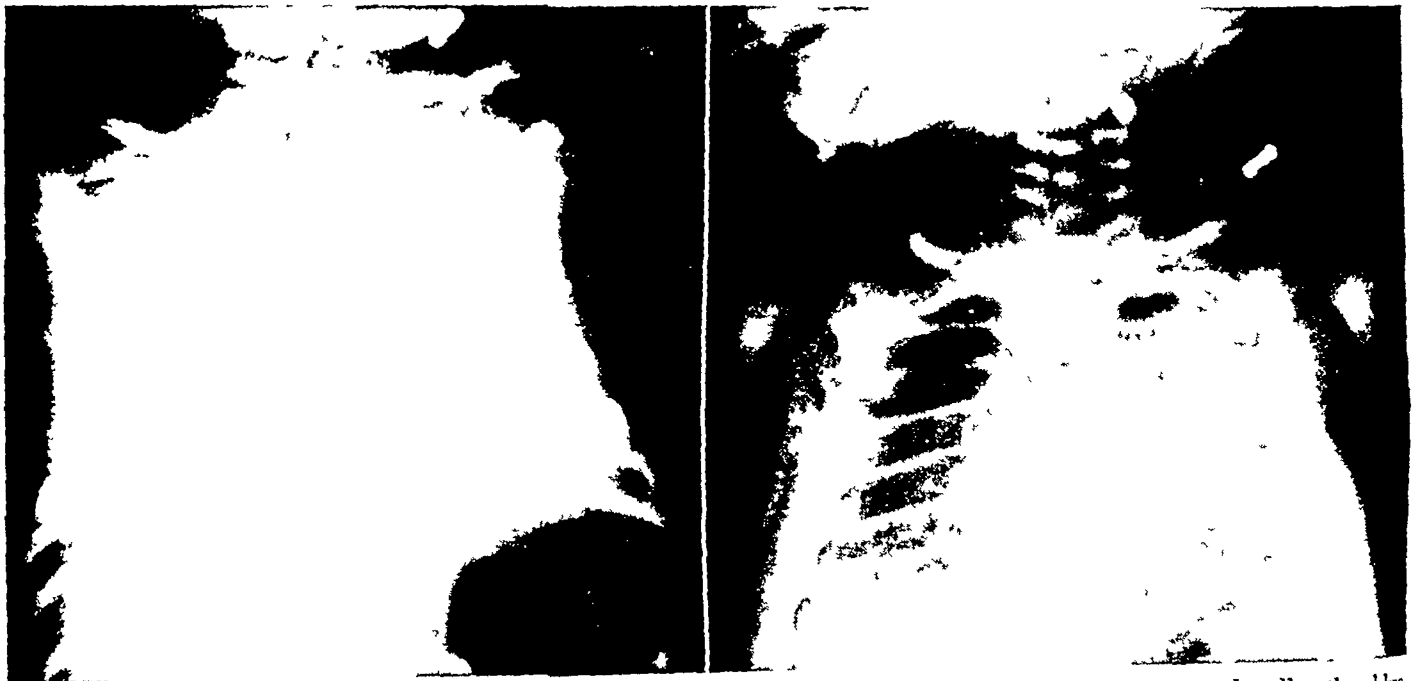
From the Anesthesia Division University of Rochester School of Medicine and Dentistry and Strong Memorial Hospital deterioration in the respiratory status occurred for several hours Thereafter, improvement was steady until discharge 10 days later Serial examinations, made until the infant reached 6 months of age revealed apparent normal psychomotor development

Comment

Respiratory distress in the newborn infant leads either to death in a few hours to a few days or to gradual recovery If an infant is premature, problems of gaseous diffusion secondary to alveolar immaturity and the inefficient structural configuration of the premature thorax combine to augment the respiratory distress[7] Because the etiology of the respiratory distress syndrome still remains obscure, management has principally been supportive Nonetheless, the clinical picture of sternal retraction, increasing dyspnea, cyanosis, and failing respirations represents a valiant and violent struggle to respire, which if unsuccessful results in death from anoxia Many have felt that physical exhaustion is a critical factor contributing to an anoxic death[8] It seems that assisting respiration offers a rational means of management until specific therapy becomes available By reducing the effort to breathe, artificial respiration may interrupt the inexorable progression from respiratory distress to failure


Left, roentgenogram of 2 hour old infant showing marked generalized increase in pulmonary density and well outlined bronchial tree *Right*, roentgenogram of infant after three days of respirator therapy showing improvement in aeration of both lungs

Whether infants with the respiratory distress syndrome have hyaline membranes during their period of distress and subsequently recover can only be a matter of conjecture Smith has noted, however, that hyaline membranes are rather sharply limited to infants born alive who die one hour to rarely more than four days after birth[7a] One may reason that either all infants with hyaline membranes die or some type of autogenous resolution of the membrane takes place If the latter is true, the hyaline membrane in the early hours and days of life represents a major but temporary respiratory handicap During this early critical period, until resolution is accomplished, assisting respiration by increasing ventilation may improve gas exchange, thereby reducing hypoxic and hypercarbic drives and respiratory effort exerted by the infant

Benson and others[1] suggested early tracheotomy, intravenous administration of curare, and induction of respiration by positive pressure Although management of this case agreed in principle with that of Benson and co workers, it differed in two important aspects Tracheostomy was avoided because mediastinal emphysema, sepsis, and pneumothorax are not infrequent problems in the infant[9] Ventilation was accomplished through an oral endotracheal tube Secondly, curare was not administered, since expansion of the infant's chest appeared adequate Benson's group, however, believed it necessary to use curare in order to reduce the high inflation pressures needed to force the infant into the rhythm of the respirator in the early period of ventilation We believe that active spontaneous respirations continuing in the early phase of treatment probably represented a continued, albeit attenuated, response of the infant's respiratory center to inadequate gaseous exchange at the alveolar-capillary level On the other hand, during later treatment, if spontaneous respirations recurred after a period of respirator induced apnea, this was often an early warning sign of an obstructed airway Endotracheal suctioning usually revealed the cause to be secretions, and after the airway was cleared apnea could be easily reduced If curare is not administered, spontaneous respiratory efforts are allowed to resume if either airway obstruction occurs or mechanical difficulties develop with the respirator

One set of blood analyses was obtained on the third day of respirator therapy At that time the values were carbon dioxide content, 23 6 mEq per

[illegible]

liter sodium level, 137 mEq per liter, chloride level, 102 mEq per liter, potassium level, 4 8 mEq per liter, and nonprotein nitrogen level, 66 mg % Further blood studies were not deemed necessary The untiring efforts of the pediatric department in managing the many problems of infant care and the constant expert nursing by personnel trained in the problems of airway management were felt to be decisive factors in the successful recovery of this patient Management was simplified by having the infant in the recovery room, where anesthesia staff members were always present

Summary

Respiratory distress occurred in an infant shortly after birth Therapy consisted of controlled respirations induced with a volume-limited, pressure-variable respirator The significance of physical exhaustion as a critical factor leading to respiratory failure was considered

Drs Alastair J Gillies and Jim E Fuller offered valuable suggestions for this study

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APLASTIC ANEMIA PRECEDING ACUTE MYELOBLASTIC (HISTIOCYTIC) LEUKEMIA

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A young woman, who had had a normal pregnancy and delivery more than a year before, was hospitalized for weakness, myalgia, pharyngitis, cough, and fever The diagnosis was aplastic anemia, the treatment included corticotropin, hydrocortisone, an antibiotic, and transfusion of whole blood After discharge and several months of improvement, there was a recurrence During the second hospitalization treatment included antibiotics, mercaptopurine, methotrexate, corticotropin zinc hydroxide, and prednisolone A second remission was obtained, during which she received five transfusions The final hospitalization was for recurrence of severe menorrhagia with ecchymoses, leukemic infiltrations of the skin, and pneumonitis, the blood picture now was that of acute monocytic leukemia The history illustrates the fact that acute leukemia is sometimes preceded by atypical manifestations, which in this case took the form of aplastic anemia

Atypical manifestations preceding the development of acute leukemia have been recognized for many years[1] That they do occur is probably not generally recognized by physicians This case report is concerned with what has been considered the classic concept of aplastic anemia as the first manifestation of acute myeloblastic leukemia The symptoms of aplastic anemia preceded the onset of hematological recognition of the acute leukemia by an interval of about 10 months It may be of interest too, because a clinical, but not a hematological, remission lasting five months was accomplished with large doses of steroids

Report of a Case

First Hospital Admission —A 23-year-old housewife was admitted on March 6, 1956, with the following history She had considered herself well until December, 1955, when she developed weakness and became easily fatigued Subsequently, she developed myalgia and pounding of the heart on mild exertion She did not see her family physician until shortly before she was hospitalized The review of systems gave negative findings except for a mild sore throat, unproductive cough, and fever for two days before admission, for which she was given a broad-spectrum antibiotic Detailed questioning failed to reveal exposure to toxic substances or ingestion of any other drug The physical examination revealed an apprehensive young woman, with mild redness of the pharynx without edema or exudate and pallor of the mucous membranes Careful search for enlarged lymph nodes, spleen, or liver gave negative results There were no petechiae or ecchymoses The past history was noncontributory In September, 1954, she delivered a normal child and the routine blood counts gave normal findings

On admission, laboratory studies revealed the following information hemoglobin level, 5 4 Gm per 100 cc, hematocrit value 17 vol %, white blood cell count, 5,900 per cubic millimeter (38% segmented neutrophils, 8% stab forms, 53% lymphocytes, and 1% monocytes, 2 normoblasts), blood type A, positive, mean corpuscular volume, 94, mean corpuscular hemoglobin, 34, mean corpuscular hemoglobin concentration 32, reticulocyte count, 0 4%, platelet count 23,400, and serum bilirubin level, 0 1 mg direct, 0 7 mg total Urinalysis gave normal findings Total protein value was 5 1 Gm, albumin level was 2 8 Gm, and globulin level was 2 3 Gm Examination of the bone marrow, as interpreted by the pathologist, was as follows "The marrow is very cellular The myeloid-erythroid ratio is 4 1 The myeloid and erythroid maturation series show no shifts in the distribution of cells The megakaryocytes are plentiful They have sharp cytoplasmic margins, decreased granulation and are not producing platelets No atypical cells are seen (except megakaryocytes) There is no evidence of malignant or leukemia cells Interpretation This probably represents a variety of aplastic anemia characterized by inhibition of platelet production and inhibition of release of red blood cells from the marrow"

A roentgenogram of the chest was reported by the radiologist as compatible with a viral pneumonitis

Hospital Course—The patient's temperature on admission was 101 6 F (38 6 C) and remained elevated until March 10, 1957 On March 9, after the indicated studies were completed and the diagnosis of aplastic anemia was established, the patient was given 80 units of ACTH gel daily, 40 mg of hydrocortisone daily, and a broad-spectrum antibiotic On the next day, the temperature became normal and there was rapid improvement generally She was given five units of whole blood On March 17, there was a mild reticulocyte response to 2 1% On the eighth hospital day, I thought I could feel the tip of the spleen, but this was the only time it was palpable until after the hematological picture changed

Other indicated diagnostic studies done during this hospital period were as follows one blood culture, which showed no growth, red blood cell fragility which was normal, nonprotein nitrogen level, 34 mg %, and first and second strength purified protein derivative tuberculin skin tests both of which were negative Almost daily, blood and reticulocyte counts were done The slight reticulocytosis was unsustained All treatment was discontinued two days before discharge There was no recurrence of fever or other symptoms Two other platelet counts were 23,400 and 21,800 respectively The day before discharge the hemoglobin level had increased to 13 6 Gm per 100 cc, the hematocrit value to 43 vol %

For the next few months, the patient did fairly well However, by July 30, 1956, her hemoglobin level dropped to 7 Gm per 100 cc, and in August she was hospitalized for two days and given four units of whole blood The white blood cell count was 7,300 with 5 stabs, 50 segmented neutrophils, 44 lymphocytes, and 1 monocyte The platelet count was 42,100, the reticulocyte count 0 3%

Second Hospital Admission, Nov 25, 1956—The patient was admitted primarily for blood transfusions, and, because the vaginal bleeding became so severe, it could not be handled on an outpatient basis Hemogram revealed the following information hemoglobin level, 6 3 Gm per 100 cc, hematocrit value, 16 vol %, and white blood cell count, 115,000 per cubic millimeter with 65% blast forms, 3% stab forms, 6% segmented neutrophils, 20% lymphocytes, and 6% monocytes The patient required almost daily blood transfusions because of the severe vaginal bleeding One week after admission, she became febrile and acutely ill The subsequent four weeks were characterized by a rapid downhill course manifested by high temperature, large ulcers of gums and buccal mucosa, melena, perirectal abscess, and pneumonia In addition, she had severe deep-seated bone or muscle pain or both which required narcotics for relief She appeared to be in the terminal phase of her illness Treatment consisted of antibiotics, 6-mercaptopurine, methotrexate (Amethopterin), corticotropin-zinc hydroxide, and increasing doses of prednisolone By Dec 21, the patient was receiving 200 mg of prednisolone by mouth daily By Dec 29, there was noticeable improvement She became afebrile, the ulcers of the mouth began to heal, the pneumonia showed resolution, and the perirectal abscess showed signs of healing Before discharge, even the distressing vaginal bleeding subsided

During the critical period, almost daily, blood studies were done By Dec 20, in response to the 6-mercaptopurine and methotrexate, the white blood cell count dropped to 16,550 and subsequently to 3,600 per cubic millimeter Two days before discharge it was 4,700 per cubic millimeter The differential picture was always that of acute myeloblastic leukemia, although as the white blood cell count dropped there were fewer blast forms, and again, there was a relative lymphocytosis

Numerous platelet counts were done, and all were 80,000 or less A bone marrow aspiration was attempted but was unsuccessful The patient was discharged on Jan 19, 1957

During the next four months she was seen at about weekly intervals in the office The prednisolone was continued in doses of 30 to 40 mg daily This period was characterized primarily by vaginal bleeding, easy bruising, at times bleeding of the gums and nasal mucous membranes, and recurrent crops of petechiae of the lower extremities On March 5, 1957, for the first time, the spleen could easily be felt, but no lymph nodes or other organs were palpable On March 22, 1957, the white blood cell count increased to 18,100 per cubic millimeter with 56% blast forms, 7% myelocytes, 11% segmented neutrophils, 2% eosinophils, and 23% lymphocytes At this time she was again started on methotrexate therapy She was given five transfusions as an outpatient during this four-month period On April 26, she developed large hematomas or leukemic infiltrations on the face, shoulder, thumb, and foot The prednisolone was increased to 80 mg daily, and 6-mercaptopurine was added to the therapeutic regimen However, on April 30, severe menstrual bleeding again started, and shortly afterwards she was hospitalized

Final Hospital Admission, May 6, 1957 —In addition to the ecchymoses or leukemic infiltrations of the skin and the vaginal bleeding, a roentgenogram of the chest on May 7 revealed pneumonitis of the lower lobe of the left lung On admission hemogram revealed the following information hemoglobin level, 12 4 Gm per 100 cc, hematocrit value, 33 vol %, and white blood cell count, 102,000 per cubic millimeter with 95% of the cells representing blast forms An aspiration of bone marrow was done on May 8 and was reported by the pathologist as follows "Bone marrow smears reveal very few platelets The cells are predominately of one type which has a large irregular nucleus and rather prominent nucleoli The nuclear border is dense and irregular, and the chromatin is rather coarse throughout the nucleus The cytoplasm is scanty and pale with fine azurophilic granulosity Granulocytic and erythrocytic cells are seen in rather markedly reduced numbers The adult erythrocytes show no defect in hemoglobinization Bone marrow sections reveal large masses of cells similar to the above but also suggesting histiocytic cell types The marrow fat is completely replaced Diagnosis acute monocytic leukemia '

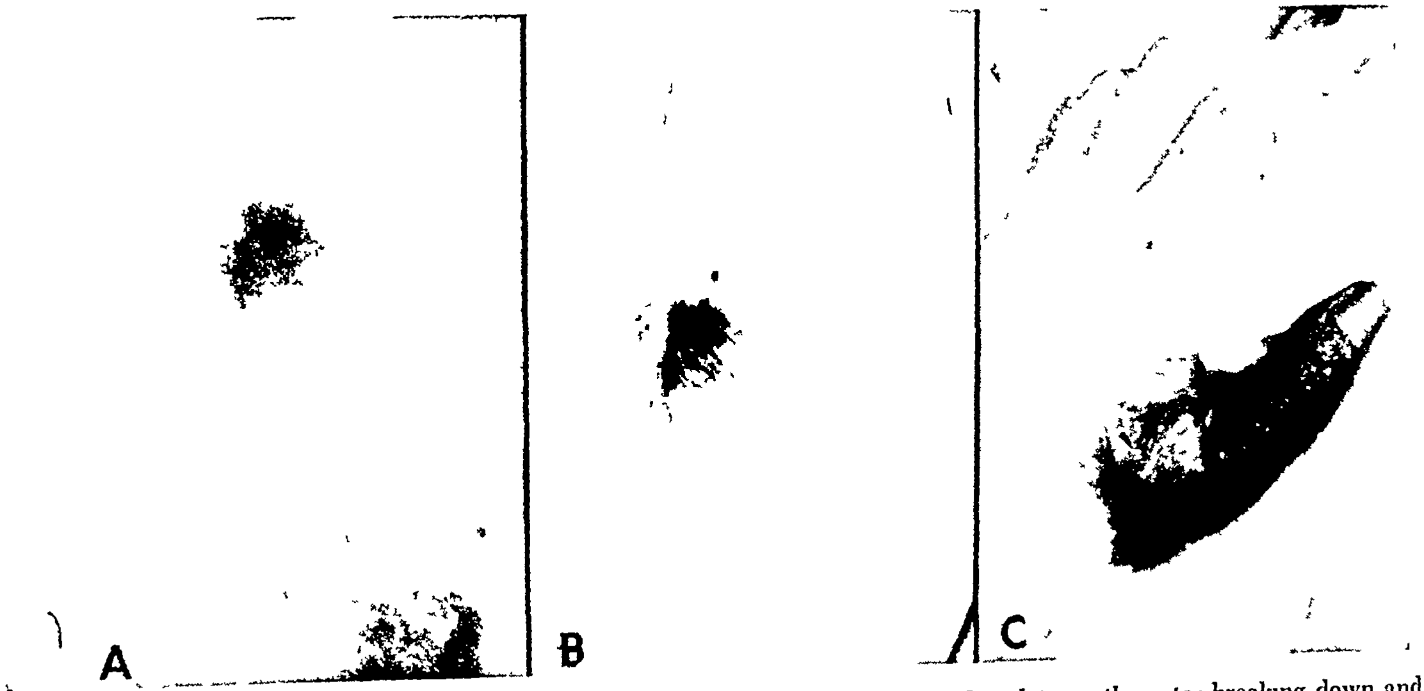
Despite all treatment which included whole blood, antibiotics, antimetabolites, ACTH, and prednisolone to 350 mg daily, and the patient's tremendous courage during the entire illness, especially during the critical periods, she died on May 31 During the last week of her illness she developed multiple subcutaneous indurated areas of the skin up to 5 cm in diameter, these had a hemorrhagic center and appeared in new crops daily The affected thumb became indurated, dark blue, and extremely painful On consultation with the radiologist, it was decided that, if this were a leukemic infiltrate of the member, a small dose of irradiation might alleviate the pain Accordingly, she was given a test dose of 200 r, but on the next day the entire digit became gangrenous The indurated, raised ecchymotic areas as they first appeared, the lesion a few days later with the center breaking down and becoming necrotic, and the gangrenous thumb are shown in the figure

An autopsy was performed The final anatomical diagnoses were (*a*) acute monoblastic leukemia (stem cell leukemia) with involvement of the spleen, liver, lung, kidneys, skin, lymph nodes, and bone marrow, (*b*) diffuse and focal hemorrhagic infarcts of the kidneys, with pelvic and perirenal hemorrhages, (*c*) gastric petechiae, and (*d*) focal bronchopneumonia The spleen weighed 550 Gm Microscopic examination revealed monoblastic infiltration of the heart, lungs, liver, spleen, adrenals, kidneys, bone marrow, and lymph nodes The latter were almost completely replaced by monocytic cells, which invaded the capsule and extended into the surrounding fatty tissue The normal architecture of the nodes was almost entirely destroyed

Comment

Wintrobe [2] prefers the term primary refractory anemia to aplastic anemia The latter term has been long associated with concept of an acellular or hypocellular bone marrow However, it is now recognized that many patients with so-called aplastic anemia have a normal cellular or hypercellular bone marrow In the peripheral blood the characteristic triad of anemia, neutropenia, and thrombocytopenia is seen in all cases of primary refractory anemia This triad of findings was present in the case herein reported In addition, there was a relative increase in normal small lymphocytes

The problem of the preleukemic stage" of acute leukemia has been extensively studied by Block, Jacobson, and Bethard [3] They reported their findings in 17 cases and reviewed the findings in 12 reported by others up to that time In all of their cases, regardless of the length of the preleukemic phase, there were clinical findings of defects of marrow hematopoiesis, e g, anemia, thrombocytopenia, leukopenia, or combinations of these They emphasized that, in their patients and in those reported in the literature, there was an abnormal hemorrhagic tendency early in the course of the disease In the preleukemia phase, most patients reported had recurrent infections, ulcerations in the mucous membranes of the mouth, and refractory anemia Block and others also emphasized that in the preleukemic phase, the diagnosis of leukemia could not be made The peripheral blood and the bone marrow showed no evidence of leukemia In a few cases in which it was done, even biopsy of the spleen or liver showed no concrete evidence of leukemia In one case, the bone marrow showed no evidence of leukemia two weeks before it became evident in the peripheral blood The diagnoses originally considered in these and other cases reported[4] were primary refractory anemia with hyperplastic marrow and acquired hemolytic anemia, toxic aplasia of the marrow and acquired hemolytic anemia, hypersplenic neutropenia and toxic neutropenia, primary or secondary thrombocytopenic purpura, nonthrombocytopenic purpura, primary or secondary aplastic anemia, hypersplenism, miliary tuberculosis with leukemoid reaction, and pernicious anemia



A, indurated, raised ecchymotic areas of leg as they first appeared, *B*, lesion few days later with center breaking down and becoming necrotic, and *C*, gangrenous thumb

Meacham and Weisberger[4] reported six cases with various combinations of anemia, leukopenia, neutropenia and thrombocytopenia with a hyperactive bone marrow The spleen was palpable in only one patient Each patient died of acute myeloid or monocytic leukemia In the cases of Block and others, none had enlargement of hematopoietic organs prior to the onset of clinical recognition of acute leukemia In none of the cases reported was it possible to establish a diagnosis initially The duration of the preleukemia phase has been reported as short as 3 months and as long as 34 months As far as can be determined all of the patients so far reported developed acute myeloblastic or monocytic (stem cell) leukemia Wintrobe[2] pointed out that it may not be correct to refer to this as the preleukemic stage of leukemia The nature of leukemia is still not understood, and another interpretation of the so-called preleukemia phase, Wintrobe states, is that they may represent a hematopoietic disorder which has changed to leukemia In three other cases reported by Meacham and Weisberger,[4] reticulum cell sarcoma developed

Summary

In the case reported here, anemia, neutropenia, relative lymphocytosis, and thrombocytopenia preceded clinical evidence of bleeding by eight months The preleukemic phase was characterized clinically by refractory anemia and recurrent infections Hematological evidence of leukemia was found 10 months after the onset of clinical symptoms The spleen was palpable on only one day of the preleukemic phase A fairly good clinical, but not hematological, remission lasting about five months was accomplished by the use of large doses of adrenocortical hormones when it appeared the illness was fatal When the patient relapsed, even larger doses of adrenocortical hormones, as well as other drugs, were ineffective The terminal illness was that of acute stem cell leukemia

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BELL'S PALSY—A MEDICAL EMERGENCY

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Sudden, spontaneous interruption of the function of the seventh cranial nerve is no longer treated expectantly It must be dealt with as a medical emergency to relieve the ischemia of the nerve in the facial canal The ischemia results from vasospasm and is aggravated by reactive edema The pathological process is that of ischemic neuritis Treatment should be started as soon after the onset of paralysis as possible, preferably within the first 48 hours It consists of blocking the stellate ganglion and administering nicotinic acid parenterally to achieve vasodilation and administering corticosteroids to reduce edema Although in most cases recovery is spontaneous, the possibility of permanent distressing sequelae, such as residual paralysis, contracture, associated movements, and hemifacial spasm makes prompt treatment essential

When you saw your last case of Bell's palsy, did you think of it as an emergency? Until recently, thoughts concerning therapy for this condition ranged from complete nihilism to the firm conviction that one of the neurotropic vitamins was a specific cure Physical therapy, consisting of heat, massage, splinting, and electrical stimulation has also been advocated Textbooks of medicine published less than 10 years ago offered no more However, an eventful revolution has occurred in the management of Bell's palsy The practical result of the radical change in therapeutic approach has been a shortened course and an improved prognosis

The new therapy employs stellate ganglion block, parenteral nicotinic acid, and administration of corticosteroids at the earliest possible moment, if this does not bring quick improvement, anticoagulant and fibrinolytic agents may be used In the few cases where these medical measures fail, surgical decompression of the facial nerve should be recommended [1]

Present Concepts

A discussion of the present-day concepts of the pathogenesis of Bell's palsy will make understandable the adoption of the new therapy Bell's palsy is a spontaneously occurring condition of unknown cause in which the function of the seventh cranial nerve is interrupted This definition excludes Ramsey Hunt's syndrome (herpes zoster oticus, which is caused by viral involvement of the geniculate ganglion),[2] and Melkersson's syndrome (peripheral facial palsy associated with facial angioedema, especially of the lips) [2]

Loss of function of the facial nerve and the muscles it innervates produces a profoundly depressing effect on the psyche [3] The person is unable to communicate by facial emotional expression, which is the universal language, he cannot illustrate speech and mood [4] The paralyzed side hangs always in the same blank state, the expressionless countenance has an ironed-out" appearance, the eyelid will not close, the corner of the mouth sags, the lips are drawn to the unaffected side, the patient is unable to whistle, smile, close his eye, or wrinkle his forehead [5] He is, indeed, a forlorn sight, yet generations of practitioners have treated Bell's palsy as a condition demanding no immediate active measures,[1a] because they did not understand its pathogenesis

The disease develops suddenly when the person is feeling perfectly well There may or may not be a history of chilling or exposure to draft Paralysis is often preceded by aching pain about the homolateral mastoid process for one, two, or more days before the palsy and, quite commonly, for 48 hours after the paralysis has developed [6] The attack rate is unrelated to sex, seasons, or geography The adult age group is most commonly afflicted Definite familial incidence has been noted There appears to be some constitutional predisposition, as evidenced by recurrences in some patients [7]

Since idiopathic peripheral palsies elsewhere in the body are virtually unknown, the physician must look to the unique anatomy of the facial nerve for a possible explanation One compelling fact is this the facial nerve traverses a close-fitting tunnel of unyielding bone from 1 cm cephalad to the geniculate ganglion to the stylomastoid foramen This is the fallopian canal which funnels somewhat at the stylomastoid foramen, the contents of the canal are tightly bound down by a fibrous connective sheath adherent to the epineurium [8] In this setting, another anatomic fact must be added The blood supply of the facial nerve within the fallopian canal has two sources (1) the petrosal artery, a branch of the middle meningeal, which supplies the horizontal portion of the nerve and the geniculate ganglion and anastomoses with the other source of supply (2) The stylomastoid artery, which, coming from the external carotid, enters the stylomastoid foramen from below and supplies the vertical portion of the facial nerve [2]

From the Calabasas Medical Center

Now that the important peculiarities of the anatomy are noted, assume that vasospasm for some unknown reason occurs and produces ischemia in the contents of the fallopian canal Prolonged ischemia, by changing the permeability of the cell walls, leads to edema, which, in the unyielding bony canal, causes compression This, of course, further reduces blood flow, aggravating the ischemia The end-result, if the vicious circle is unchecked, is necrosis and, finally, fibrosis[9] Bunnell[10] pointed out that similar tight-fitting situations are well known, as in contusion of the brain, injury to the volar aspect of the forearm leading to Volkmann's ischemic contracture, a hand in a tight plaster cast, and finally a tendon in the annular ligament of the finger

Most authorities are now agreed that Bell's palsy is an ischemic neuritis resulting from segmental arteriolar spasm,[7] a "vascular dysregulation,"[2] which produces secondary edema, that the vasa nervorum in this location are, in effect, end arteries[7] In addition to spasm, there may be an element of thrombosis[1b]

The degree and duration of ischemia determine the course and prognosis Lesser degrees of ischemia cause partial or incomplete paralysis The integrity of the axons is preserved, so there is no reaction of degeneration[8] The course is short, often less than one week Every patient with this mild type recovers spontaneously and completely[1b]

Severe degrees of ischemia lead to complete paralysis, nevertheless, 80% of these patients recover fully with no sequelae In these cases wallerian degeneration occurs, but, because the neurilemmal sheaths remain intact, the axons regenerate perfectly[8] The course is longer, recovery begins in one to three weeks and is complete in four to six weeks[1b] The remaining 20% of the patients make variable incomplete recoveries over three to nine months, with some sequelae in every case[1b] Regeneration is delayed for some reason, possibly continuing ischemia or compression, or both With delay, the neurilemmal sheaths collapse or are filled with proliferative scar[8] The regenerating axon is blocked If the obstruction is complete, the muscle innervated by that axon remains paretic and recovery is, to that extent, incomplete This muscle is eventually replaced by fibrous tissue and contracture develops Such shortening may tend to restore facial symmetry at rest, but the affected side of the face remains immobile during emotional expression[11]

If the obstruction in the neurilemmal sheath is incomplete, the axon may grow around the block and find passage in a different, patent sheath This perverted recovery results in associated movement or synkinesis, which is the involuntary contraction or overaction of one part of the face during the voluntary contraction of another part For example, there may be an involuntary twitch of the angle of the mouth each time the eyes are blinked[11] The "crocodile tear" phenomenon is a special form of associated movement Unilateral paroxysmal lacrimation occurs on eating This is thought to result from a shunting of the axons which normally ended in the tongue (via the chorda tympani) to the lacrimal gland (via the greater superficial petrosal nerve)[11]

Another sequela is hemifacial spasm of the affected side of the patient's face, the features of which are irregular, tonoclonic contractions of muscles from frontalis to platysma, notably those at the eye and the mouth[12]

These residuals, namely, persistent paresis, contractures, associated movements, and hemifacial spasm occur commonly They change the physiognomy of the person and his outlook on life[3] Their prevention is the goal of therapy[1b] Therefore, in every case of Bell's palsy, the safe procedure is to presume that there will not be complete recovery unless something more than an attitude of masterly expectancy is adopted,[8] and, conversely, that disfiguring sequelae will result unless treatment is urgently undertaken and vigorously pursued[1b]

New Therapy

With the next case of Bell's palsy, consider adopting the following method Establish the diagnosis by exclusion of supranuclear lesion (which spares the occipitofrontalis, orbicularis palpebrarum, and corrugator supercilii muscles), pontine lesion (which involves the ipsilateral pyramidal tract), pontomedullary lesion (indicated by ipsilateral internal strabismus because of involvement of the sixth cranial nerve and crossed motor weakness because of involvement of the contralateral pyramidal tract), middle ear disease with hearing disturbance, labyrinthine disease with disturbance of equilibrium, herpes zoster oticus with the typical eruption about the ear, and trauma by history[4]

Immediate stellate ganglion block should be obtained with 10 ml of 1% procaine hydrochloride (For detailed technique, see Moore's monograph[13]) Swan[14] first reported success with this modality of treatment Korkis[1] repeatedly has stated that early stellate or cervical sympathetic block is associated with rapid improvement and, in these cases, the incidence of complete recovery is greater Such success confirms Kettel's[2] theory of "vascular dysregulation" The correlation is direct, many patients undergoing block immediately show visible increase in tone and partial return of motor function[15] Corticosteroids, such as dexamethasone (Deronil), in doses of 0 75 mg four times daily, should be started in an effort to reduce secondary edema

Nicotinic acid given parenterally appears to have real merit in treating Bell's palsy Kime[5] told of excellent results obtained in 74 consecutive patients treated from 1947 to 1957 He used daily intramuscular injections of nicotinic acid (unmodified) The doses, made large enough to produce flushing ranged from 100 mg to 250 mg Supplementary orally given nicotinic acid was used A good combination containing 250 mg of nicotinic acid along with thiamine, pyridoxine, and ascorbic acid (Liponicin) is available Of the 74 cases, 39 were treated within two days of the onset of paralysis In every one of these, there was beginning movement within a week and complete recovery within two weeks

In addition, the author observed "a *pallor syndrome* seen in many of these patients at the peak of the flushing The paralyzed side of the face will not flush like the normal side and gives an impression of pallor in the area of the distribution of the external maxillary artery This is usually seen on the first few injections and will disappear as total flushing occurs The pallor diminishes in size and usually disappears after the third or fourth injection, and the face flushes evenly thereafter" Within 24 hours improvement in tone will be noted, followed by 60% return of function within a week, and full recovery during the following week[5] Weiner and others[16] have recently shown in animal experiments a fibrinolytic effect in nicotinic acid given parenterally Its adjunctive use may, therefore, serve to open thrombotic vessels

Administration of human fibrinolysin (Actase) might be considered in older persons, in whom the likelihood of thrombosis is greater (This is speculative, no prior recommendation to this effect having been noted in the literature) Anticoagulants, warfarin (Coumadin) sodium, or heparin (Neoheprin), should be used where thrombosis is suspected either as the primary cause or secondary to prolonged vasospasm[1b]

Decompression of the facial nerve in the fallopian canal with meticulous neurolysis should be recommended when all medical efforts fail[17] This procedure is performed by otolaryngologists with use of a dissecting microscope and dental drills It is indicated where there has been no improvement, where there has been incomplete recovery and in cases of relapse The striking fact is that recurrence on the side of the decompression is unknown[8]

Supportive measures are important Galvanic stimulation of the paralyzed muscles should be demonstrated to the patient and he should obtain a stimulator for his use at home three times daily This maintains the muscles in a more nearly normal state while the time for reinnervation passes A sling of cellophane tape to support the paralyzed muscles can be applied by the patient after instruction by the doctor This minimizes stretching by the normal muscles of the opposite side and by gravity Through this splinting the lower lid can be reapproximated to the globe, checking the overflow of tears Massage should be carried out, and an eye patch should be worn to prevent xerophthalmia

Since ischemia is the main operative factor in Bell's palsy, the physician may be tempted to utilize oxygen, this is probably not wise in view of the cranial vasospastic effect that oxygen sometimes has, e g, the occasional migraine sufferer who obtains relief from the pain caused by vasodilation by breathing pure oxygen[18]

Summary

Bell's palsy is a medical emergency It results from vasospastic ischemia, or thrombosis (rarely), or a combination of both Treatment is aimed at vasodilation and reduction of secondary edema with the use of a stellate ganglion block without delay, administration of corticosteroids, and nicotinic acid given parenterally with the orally given supplement Thrombosis, if suspected, is treated with anticoagulants and, possibly, with fibrinolysin Surgical decompression and neurolysis is recommended when recovery is incomplete or relapse occurs Therapy which is started immediately and pursued vigorously shortens the course of the disease and greatly improves prognosis

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COUNCIL ON MEDICAL PHYSICS

Report of the Council

The Council has authorized publication of the following report

RALPH E DE FOREST, M D, *Secretary*

EVALUATION OF ELECTRICAL MUSCLE STIMULATION IN PROVIDING PULMONARY VENTILATION

This report considers the concept of controlling respiration and producing pulmonary ventilation by the electrical stimulation of respiratory muscles or their nerve supply

Data available to the Council on Medical Physics cover the use of electrical current for stimulating innervated skeletal muscles by applying electrodes (1) to the phrenic nerve directly or to the skin of the neck in the region of the phrenic nerve, (2) to the skin of the epigastric area, and (3) to the skin of the lower costal borders of the thorax and/or the abdomen just below the level of the umbilicus

Data evaluated by the Council at this time cover only the use of electrical currents capable of eliciting contraction of muscles which have an uninterrupted nerve supply

Physiology

A number of factors must be considered in assessing adequate ventilation of the lungs Among the most important of these are (1) rate of respiration, (2) magnitude of the tidal volume, (3) volume of the total dead air space, and (4) minute volume

The average resting adult has a respiratory rate of 15 to 20 cycles per minute The tidal volume of the average resting adult is about 500 cc, it is the volume of air which is inspired or expired during each respiratory cycle The total dead air space is that space which, just prior to expiration, contains all the air which did not come into contact with alveolar respiratory epithelium Most of the dead air space volume (about 150 cc) is contained in the mouth, pharynx, larynx, trachea, and bronchi It is, therefore, readily apparent that in order to provide adequate pulmonary ventilation the volume of air inspired must at all times be in excess of the dead air space volume The respiratory minute volume is another unit useful in assessing pulmonary ventilation, it is the total volume of air inspired or expired during one minute Since the average adult inspires about 500 cc of air per respiratory cycle and this cycle occurs 15 to 20 times per minute, the average adult minute volume ranges from 7 5 to 10 liters of air

The chief muscle of inspiration is the diaphragm, which at times is assisted by the intercostales externi, sternocleidomastoidei, levatores scapulae, as well as the anterior serrati and scaleni The chief muscles of expiration, on the other hand, are the abdominals which can be assisted by the intercostales interni and the posterior inferior serrati

Stimulation of the Phrenic Nerve by Electric Current

Currents used to stimulate the phrenic nerve in the neck are characterized by frequencies ranging from 40 to 60 cycles per second[1] Duration of one impulse ranges from two to four milliseconds The minimum voltage needed to elicit the necessary contraction of the diaphragm varies in individual patients However, according to one report,[2] the stimulating current does not exceed 40 volts According to other reports,[3] it was found possible to provide adequate pulmonary ventilation by stimulating one phrenic nerve only The reason given for this is that when one phrenic nerve is stimulated, the diaphragm on the stimulated side contracts and lowers the intrathoracic pressure in that portion of the chest, the mediastinum then shifts toward the stimulated side, thereby decreasing the intrathoracic pressure in the nonstimulated side and allowing air to enter that portion of the chest

Adequate pulmonary ventilation and arterial oxygen tension were produced in dogs, cats, and monkeys which had been paralyzed to the point of apnea by means of spinal anesthesia with procaine hydrochloride[4] Artificial respiration by phrenic nerve stimulation has also been reported in cases of respiratory failure secondary to postmeasles encephalitis,[5] asphyxia neonatorum, chronic asthma, and bulbar poliomyelitis[6]

In 29 cases of asphyxia neonatorum, 25 infants responded to electrophrenic respiration, whereas the 4 infants who did not respond died from causes not involving pulmonary pathology[7] Attempts to improve respiration by phrenic nerve stimulation in 29 asthmatic patients showed only reduced respiratory effectiveness[8] This result was explained on the basis of inefficient diaphragmatic action, due to intrinsic weakness of the diaphragm or dominance of the costal respiratory musculature Among six patients with bulbar poliomyelitis studied, electrophrenic respiration was effective in causing irregular breathing to be replaced by normal, regular breathing rates [9] Another investigator [6] had similar results in two cases

Difficulties can be encountered in the attempt to improve respiration by electrical stimulation of the phrenic nerve, and, for this reason, the procedure is infrequently used The operator may find it difficult to locate percutaneously the motor point of the phrenic nerve in order to place the electrode on the neck so that it will effectively stimulate the phrenic nerve Also, when using a surgical approach, he may find it difficult to locate the phrenic nerve for direct application of the electrode to the exposed nerve Thus, as a rule, this technique is used only by those physicians highly skilled in its application

Application of Electrodes to Skin of Epigastrium and Lower Abdomen

Information available to the Council on the application of electrodes to skin of the epigastrium and lower abdomen was obtained from laboratory investigation, clinical use, and reports by lay emergency rescue squads

An active electrode is placed on the skin in the epigastric or xiphoid area, and a dispersive (indifferent) electrode is placed on the skin of the back in the upper thoracic region to complete the electrical circuit Stimulating current is applied to the person at the rate of 18 to 22 surges of current per minute

Reports from Emergency Rescue Squads—The following reports concern the application of electrical currents to the skin of the epigastrium and lower abdomen in cases of emergency for artificial respiration and resuscitation These reports are of essentially the 'eye-witness" type, which, by their very nature, can give only incomplete information

CASE 1—A middle-aged woman who had ingested an unknown quantity of chloral hydrate was unconscious when found, and her breathing was shallow at the time electrical currents were applied Her color was good Respiration was 'maintained well" by the application of electrical stimulation Oxygen was administered to the subject while she was being transferred to a hospital

CASE 2—A 55-year-old man, with a history of cardiac disorder, was unconscious and cyanotic when the rescue squad arrived After electrical current was applied, the cyanosis disappeared rapidly, and the subject regained consciousness within five minutes

CASE 3—A 42-year-old woman was pinned in the car in an automobile accident She had suffered 'crushing injuries' and was unconscious Her color improved after stimulating current was applied, she regained consciousness after 35 minutes of resuscitation efforts and was then removed from the car

Two other rescue squads reported summaries of the results obtained by the use of this method of artificial respiration and resuscitation 1 One squad obtained satisfactory results on the five occasions that this method was used 2 The other squad obtained varying results with the use of this method on 13 subjects However, information furnished by these two rescue squads regarding the state of respiration, or illness or injury in all of these subjects was incomplete

Results of Laboratory Experiments—Reports of a series of laboratory experiments available to the Council show the following results 1 Electric current applied to the epigastric area of a normally breathing person caused the tidal volume to be in excess of 1,000 cc 2 Diaphragmatic excursions of a normally breathing person could be made to coincide with application of electrical stimuli 3 An animal subjected to varying doses of thiopental (Pentothal) sodium and pentobarbital (Nembutal) consumed more oxygen while receiving electrical stimulation than while receiving manual artificial respiration 4 In four human subjects tested, contraction of the diaphragm and elevation of the rib cage were produced in response to electrical stimuli applied to the anterior abdominal wall at the xiphosternal junction, inspiration occurred during the time that the stimuli were applied, expiration, at the cessation of stimuli Both normal and abnormal subjects were tested No other information concerning subjects was given No data on ventilatory volumes were provided (other than listed under 1)

A group of investigators [10] reported results of experiments in which a total of six dogs and five rhesus monkeys received electrical stimulation in the following manner All animals were first subjected to either Sarin vapor (GB vapor), curare, pentobarbital, or a combination of curare plus pentobarbital Sarin, or isopropyl methyl phosphonofluoridate, is also known as nerve poisoning gas

The six dogs were divided into two groups of three dogs each After the first three dogs had been exposed to Sarin vapor, vigorous muscular contractions, synchronous with applied electrical stimuli, were obtained However, no appreciable volume of air was moved into or out of the lungs The other three dogs received either pentobarbital or curare or a combination of the two Tidal volumes were not appreciably altered in the first dog which was given pentobarbital but was breathing spontaneously Only spastic chest movements, with negligible pulmonary ventilation, were obtained in the other two dogs, one of these received curare, and the other received intravenous injections of curare plus pentobarbital in quantities just sufficient to stop respiration

All five monkeys tested were exposed to Sarin vapor for one minute Four of them were given intramuscular injections of atropine (2 mg per kilogram of body weight) one-half to three minutes after exposure to the gas In spite of electrical stimulation, all animals died due to lack of pulmonary ventilation

Data from two other laboratory investigations concerning respiratory volumes elicited by electrical stimulation applied to the skin of the epigastric and xiphoid areas of human subjects were also made available to the Council In the first investigation, six persons were anesthetized with thiopental sodium A spirometer was coupled in series with the anesthetic machine in order to measure applicable volumes of air Several minute-volume recordings were made to determine the average minute volume of each subject The subjects were then hyperventilated for a period of one minute, and the ensuing period of apnea was measured Later, the subjects were again hyperventilated for a period of one minute, and stimulating current was applied during the ensuing apnea Results for each case in the investigation are briefly outlined in table 1

TABLE 1 —*Results of Electrical Stimulation Intended to Produce Artificial Respiration*

Case*	Age Yr	Average Minute Volume Liter, Min	Period of Apnea After Hyperventilation of 1 Min Sec	Gas Movement During Apneic Period Liter/Min †	Remarks
1	65	4 2	90	2 8	Measurable exchange of air did not appear until 30 sec after stimulation was applied increased intensity of stimulation did not change effect
2	64	4 5			Patient developed laryngeal spasm, procedure discontinued
3	40	4 0	80	0 1	Marked stimulation of intercostal and recti muscles only 100 cc of air movement active electrode was tried in various locations
4	29	4 2	65		No air movement during measured period of apnea, stimuli continued patient resumed breathing out of phase with stimuli
5	29	5 2	75	1 0	
6	33	4 3	90		With patient breathing (no apnea) stimulation was applied for 1 min to measure possible increase of gas volume volume obtained was 4 1 liter/min

* All patients were women

† Stimulator on

Four adult men were chosen as subjects in the other investigation The investigation was divided into three major parts, and a series of three separate findings were obtained (table 2)

First, resting tidal volumes were obtained and then compared with resting tidal volumes of the same subjects while they received electrical stimulation, even though they were conscious and breathing normally Results obtained showed that tidal volumes during the period of stimulation exceeded normal tidal volumes but that breathing was not in phase with application of stimuli Next, all subjects were anesthetized with thiopental sodium, and tidal volumes were again determined These findings were then compared with tidal volumes obtained while the subjects were anesthetized but receiving electrical stimuli Results here showed an increase of tidal volumes in all cases Finally, the subjects were anesthetized in the manner described previously and were rendered apneic by hyperventilation before receiving electrical stimuli Results showed that less than dead air space volumes were moved in 17 of a total of 24 trials (Only expiratory ventilation was measured during the period of apnea)

Application of Electrodes to Thoracic Cage and Lower Abdomen

In applying electrodes to the thoracic cage and lower abdomen, two electrical circuits are utilized Stimuli intended to elicit inspiration are applied to the subject by means of two band or ribbon electrodes placed about the chest so that they pass anteriorly from the level of the xiphoid area along each side of the thoracic cage and parallel the course of the diaphragm Stimuli intended to elicit expiration are applied to the subject by means of plate type electrodes placed on the abdomen over the rectus abdominis muscle, about three finger widths below the level of the umbilicus All electrodes are held in place by rubber straps

The thoracic electrodes are to stimulate the diaphragm to cause or aid inspiration, the abdominal electrodes are to stimulate the anterior abdominal musculature to cause or aid expiration Flow of stimulating current alternates between the abdominal and thoracic electrodes [11]

Success was claimed for this technique when it was utilized in a number of patients with bronchial asthma and emphysema, a patient suffering from an overdose of sleeping tablets, who was comatose yet breathing, and a patient with acute ascending spinal paralysis (Landry's paralysis) [11]

The method has also been used as an aid in teaching breathing exercises to patients with asthma and emphysema and cerebrospastic patients receiving speech therapy [12] By adjusting the strength and duration of currents intended to elicit inspiration and expiration, attempts were made to develop coordinated effective breathing patterns [13] Eight aphasic children received 25 minutes of therapy a day for 26 weeks in order to improve respiration [13] Improved speech, it was reasoned, would follow improved respiration The author reported that a reduction in respiratory rates and an over-all increase in vital capacities were observed In addition, the over-all intelligibility of a 51-word passage read by the patients was increased Furthermore, an improvement in the articulation in counting from 1 to 10 and an improvement in the length of the vocalization of "ah" were observed

Another series of studies was conducted on 34 patients to determine the efficacy of electrical stimulation[14] The patients selected were primarily those who had not responded to other therapeutic measures, each patient received periods of therapeutic exercises combined with electrical stimulation Diaphragmatic excursions and ventilatory measurements of each patient were determined before and after completion of the series of treatments All patients readily accepted the electrical stimuli and showed no adverse effects

In five patients with chronic, previously drained empyema, the maximum amount of air which each patient could inspire per breath or per minute increased in all patients, however, this remained abnormally low in two patients Seven patients with chronic hemothorax, who had received needle-type aspiration or closed-tube drainage, showed improvement in diaphragmatic mobility and maximal breathing capacity In nine patients who had recently been treated by lobectomy and who had elevated and fixed diaphragms on the operated side, mobility of the diaphragm was improved in most cases, and an increase in maximal breathing capacity was reported In 13 patients suffering from chronic obstructive pulmonary emphysema, small but statistically significant improvements in maximal breathing capacity and vital capacity were claimed Some improvement in diaphragmatic mobility was obtained in all but 1 of the 31 patients on whom satisfactory roentgenograms were available Satisfactory roentgenograms were not available on three patients, and improvement in diaphragmatic mobility could not, in these cases, be accurately determined

It was difficult, if not impossible, to acquire a series of comparable untreated patients to serve as controls For this reason, it is equally difficult to determine how much of the improvement reported could have been obtained by the use of therapeutic breathing exercises alone or the extent to which electrical stimulation may have augmented the therapeutic breathing exercise program

In another investigation,[15] this technique of electrical stimulation was applied to eight normal healthy men The investigation was divided into two parts During the first part, vital capacities and tidal volumes were determined Stimulating current was then applied, and strength of current was increased in steps Results showed that a moderate amount of stimulation resulted in some increase in tidal volumes However, with increased strengths of current, a forced expiration resulted, with spastic contractions of abdominal musculature Currents of sufficient strength to cause a small amount of diaphragmatic activity produced an unpleasant, painful sensation So long as respiratory rates remained at a normal level, the subjects tended to synchronize breathing with the stimuli received

During the second part of the investigation, the same eight men were utilized to determine the effectiveness of this technique under the following conditions (1) anesthetized with intravenous injections of thiopental sodium but breathing spontaneously, (2) anesthetized with intravenous injections of thiopental sodium and rendered apneic by means of curare, and (3) anesthetized with intravenous injections of thiopental sodium and hyperventilated until apneic Investigators found that the breathing of these subjects when anesthetized—but breathing spontaneously—tended to coincide with electrical stimuli, provided stimuli were cycled at approximately the same rate as the breathing rate of the subjects However, respiration could in no way be controlled by application of stimuli Finally, pulmonary ventilation was not elicited with this technique during apnea produced either by administration of curare or by hyperventilation

TABLE 2 —*Effects of Electrical Stimulation Intended to Produce Respiration in Human Subjects*

	Condition of Subject	Area of Electrode Application	Amplitude Setting of Electrical Stimulator %	Tidal Volumes in Four Adult Male Subjects Cc /Cycle			
				A	B	C	D
1	Conscious normal resting			550	350	450	525
	Electrical stimulation applied	Epigastrium	50	650	425	475	550
			75	700	1100	650	600
		Xiphoid	50	850	525	650	550
			75	900	1100	850	600
2	Anesthetized with thiopental sodium			350	350	425	500
	Anesthetized with thiopental sodium and electrical stimulation applied	Epigastrium	75	650	450	450	650
			100	600	500	550	700
		Xiphoid	50	850	350	450	600
			75	800	425	600	625
			100	800	900	700	650
3	Anesthetized with thiopental sodium plus hyperventilation to apnea electrical stimulation applied*	Epigastrium	50			50	
			75	100	50	100	100
			100	300	200	225	250
		Xiphoid	50			25	
			75	25	75	75	50
			100*	150	100	175	200

* All ventilation during apneic state was expiratory

Comment

This technique, stimulation of the phrenic nerve by electric current as a means of providing artificial respiration, may be effective so long as the phrenic nerve is intact It is essential, in any case, that sufficient nerve fibers are functional in order to stimulate enough of the diaphragmatic musculature to provide adequate contraction This method is not effective if myoneural junction conduction is altered such as occurs with use of Sarin or curare and similar preparations A lesion of the lower motor neuron, which results when the phrenic nerve or its anterior horn cells or nerve roots are rendered nonfunctional, reduces all or a part of diaphragmatic musculature to a denervated state The conditions in which this technique has been found useful generally fall in the category of "upper motor neuron" lesions Difficulties encountered in locating the motor part of the phrenic nerve percutaneously or surgically have prevented the widespread use of this technique Its use in emergency situations by lay personnel is seldom attempted because of (1) the difficulty in locating the motor part of the phrenic nerve and (2) the necessity of making a proper diagnosis concerning the site of the lesion and magnitude of the paralysis-producing lesion The latter is essential to determine if the technique may be expected to be of help

Experimental studies on human subjects indicate that the application of electrodes to the skin of the epigastrium and lower part of the abdomen is ineffective in producing pulmonary ventilation in anesthetized subjects rendered apneic by hyperventilation Furthermore, the method cannot be expected to resuscitate subjects rendered apneic by curare or Sarin vapor since these drugs interfere with nerve-impulse conduction across the myoneural junction Application of stimuli to subjects capable of breathing spontaneously does not constitute an accurate means of assessing potential efficacy of these stimuli as applied to nonbreathing patients Although reports from lay rescue or emergency squads are sincere, they do not give the type of medical information necessary to determine effectiveness of the technique when it is used on asphyxiated, apneic patients In the opinion of the Council, evidence available to date does not support the case for the use of this method of applying electrical currents to produce pulmonary ventilation in nonbreathing patients Evidence regarding the application of currents to the normal person breathing spontaneously or the anesthetized person shows an increase in the respiratory minute or tidal volumes of the tested subject More evidence regarding the degree of increased respiratory tidal or minute volumes provided by use of this technique to persons comatose from disease or injury is needed before benefits to such patients can be clearly established

Application of electrodes to the thoracic cage and lower part of the abdomen has been used as an aid to teaching therapeutic exercise to patients with various types of pulmonary pathology and in speech therapy for cerebrospastic patients Evidence does not show the method to be effective in providing pulmonary ventilation in subjects with apnea due to hyperventilation or use of myoneural junction blocking agents Failure due to use of myoneural junction blocking agents is to be expected, since an intact nerve supply is necessary for the types of current used to produce muscular contraction The method appears to have merit for the teaching of breathing exercises Evidence does not show that the electrical currents actually stimulate the diaphragm to contract However, they probably are effective as signals which indicate to the subject when to perform various parts of the breathing process

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report
H D Kautz, M D, *Secretary*

CURRENT STATUS OF DIAGNOSIS AND THERAPY OF ENCEPHALITIS

Gerald M Silverman, M D, New York

Encephalitis is a primary inflammatory process in the brain, with resulting disturbance of brain function For clinical purposes, the disease can be said to be infectious or postinfectious For the most part, the infectious encephalitides are caused by intracellular parasites viruses and, less commonly, rickettsiae The great epidemic of encephalitis in the 1920s (the so-called von Economos type of encephalitis) is believed to belong in the virus infection group, although no agent was ever isolated[1] All of the bacterial, mycotic, treponemal, and parasitic meningitides can cause an associated encephalitis in the underlying brain, but these are generally classified with the meningitides The postinfectious encephalitides are believed to represent damage to the nervous system as a part of an allergic response to a preceding infection, usually viral The entity of postvaccinal encephalitis, similar clinically and pathologically to postinfectious encephalitis, is an occasional complication of vaccination with a virus vaccine (i e, smallpox, rabies)[2]

The main clinical finding in encephalitis is impairment of consciousness, usually in association with systemic signs of infection The alterations in brain function in encephalitis are in no way specific for infection They are similar to the alterations seen in diffuse encephalopathy from any cause, as, for example, the metabolic encephalopathy of diabetic acidosis, uremia, or carbon dioxide retention and the cerebral edema of massive vascular accidents or head trauma The brain has only a limited number of ways in which damage may be manifest, and so the diagnosis of encephalitis as opposed to other encephalopathy depends on finding additional evidence of primary central nervous system inflammation Such evidences can be of the following types (1) signs of an infection with known neurotropic tendencies (e g, mumps, infectious mononucleosis, Coxsackie myalgia), (2) occurrence in a postinfectious setting, (3) elevated spinal fluid cell count, (4) isolation of virus from spinal fluid, (5) isolation of neurotropic virus from nasopharyngeal or fecal material, and (6) serologic identification of neurotropic virus or rickettsia in paired (acute and convalescent) serums

The laboratory identification of viruses takes considerable time and, thus, cannot help the clinician in the acute period of the patient's illness Early diagnosis depends on bedside findings and basic clinical laboratory work

Etiology

In many cases of sporadically occurring encephalitis, a specific etiological diagnosis cannot be made, even with the help of the best laboratories[3] Clinical diagnosis is sometimes possible because of the associated signs, such as enlarged salivary glands, chest wall pain, a specific exanthem, elevated heterophil titer, or x-ray evidence of viral pneumonia (as occasionally seen in lymphocytic choriomeningitis) In epidemics, the diagnosis of individual cases can be made presumptively if the clinical signs are similar to the "lead' cases When such clinical and epidemiologic signs are not present, the specific infectious agent can be identified in less than half the sporadic cases In those cases in which the organism can be identified, the agents most commonly found are those familiarly referred to as causes of the 'aseptic meningitis syndrome' Encephalitis, when caused by these agents, is an intensification of the pathological and clinical entity of "aseptic meningitis'—meningitis without identifiable organisms in the gram stain or bacterial culture of the spinal fluid[4] Since the meninges and brain are contiguous, the distinction is often difficult The situation is comparable to that in infectious pericarditis, in that there is nearly always an associated myocarditis

In the group that can presently be identified by clinical and laboratory methods, the most common agents are mumps, measles, chickenpox, German measles, infectious mononucleosis, viral hepatitis lymphocytic choriomeningitis, herpes simplex,

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Instructor in Medicine Cornell University Medical College herpes zoster, anterior poliomyelitis, Coxsackie viruses, the growing group of ECHO viruses, and the arthropod-borne encephalitis viruses (Western equine, St Louis, and Eastern equine, in the United States) Leptospirosis, syphilis, trichinosis, scrub typhus, Rocky Mountain spotted fever, and other specific nonviral agents that can cause meningoencephalitis are not considered here "Epidemic neuromyasthenia" shows features like those of encephalitis, but its etiology requires further definition Progessive leuko-encephalopathy, a demyelinative disease sometimes associated with lymphomas, is probably of nonmicrobial origin In rare instances, acute multiple sclerosis can mimic infectious encephalitis

Postinfectious encephalitis is an uncommon complication which may follow the viral exanthems, smallpox and rabies vaccinations, influenza, pertussis, and possibly other infections[5]

The list of primary infectious and postinfectious causes is necessarily incomplete, for not only are there many agents not yet identified but, also, there is the probability that many viruses whose primary tropism is not the nervous system can become neurotropic Psittacosis and erythema infectiosum (one of the less common exanthems) are examples of this

Pathology

In encephalitis the brain is hyperemic and edematous This is most notable in the arthropod-borne group Hemorrhages are rare The cardinal features of the infectious group are mononuclear meningeal inflammation, perivascular lymphocytic infiltration, and parenchymal destructive lesions

The infectious and postinfectious types differ in three respects 1 The infectious type represents direct invasion of the brain The postinfectious type is assumed to be allergic in nature and usually has its onset 8 to 10 days after an acute systemic infection 2 The infectious type involves mainly the gray matter, the postinfectious, the white matter 3 The infectious cases show perivascular lymphocytic infiltration, the postinfectious group show perivascular demyelination

Among infectious encephalitides due to viruses, the distribution of the lesions is of interest[6] The arthropod-borne encephalitides inflict greatest damage in the region of the basal ganglions Herpes simplex involves mainly the cortex In polioencephalitis, the lesions can be anywhere in the brain but especially in the brain stem These are general tendencies, however Specific etiological diagnosis depends on the isolation of virus from the nervous system or a rise in specific antibody titer in the serum

Clinical Features

In encephalitis there is usually evidence of systemic infection, i e, malaise, fever, fatigability, an appearance of acute illness, and, sometimes, 'toxicity" Constitutional symptoms can range from moderate generalized weakness (out of proportion to the fever) to severe prostration Fever may be absent in elderly or debilitated persons The patient usually has headache due to inflammatory involvement of pain-sensitive structures inside the head, mainly the meninges and the blood vessels at the base of the brain Though fever and headache are most often present, they are not always pronounced There is always some disturbance in consciousness and in the highest integrative functions, this disturbance being the key element in invoking the diagnosis of encephalitis It may be slight, such as an exaggerated wish to be left alone, or it may be very gross, with clouding of the mind, disorientation, loss of recent memory, sleepiness, stupor, and coma Occasionally reported are a feeling of lightheadedness, even when lying down, unusual dreams, and sudden awakening at night in a state of bewilderment, which requires undue time to dispel Convulsive seizures are common, from focal myoclonic jerks to major convulsive episodes, with even further impairment of consciousness and sometimes with impairment of respiration Seizure activity may be manifested only by rolling of the eyes upward and to one side (as in an oculogyric crisis of postencephalitic Parkinsonism) or by twitching of the face In very severely ill patients, one may see the peculiar combination of unconsciousness on the one hand and simultaneous thrashing or seizures on the other The neck may or may not be stiff Unsteadiness of gait is sometimes seen[7] Nystagmus occurs, but this is infrequent Conjugate deviation of head and eyes to one side sometimes occurs, with or without seizures Impairment of eye movements is occasionally found in current experience and was a very common finding in the epidemic of "von Economo's encephalitis" Aphasia occurs, but this is, fortunately, rare Pyramidal system involvement, with hyperreflexia and extensor plantar responses, is common and may even progress to hemiplegia Weakness of limb and trunk muscles due to anterior horn cell involvement in the cord is rare, in contrast to its great frequency in spinal poliomyelitis However, instances of cord damage, with anterior horn cell involvement, was described in the 1952 California outbreak of Western equine and St Louis type encephalitis[8] Cortical and long-tract sensory disturbances may occur Changes in the abdominal reflexes are not predictable Hyperthermia, respiratory failure, shock, and arrhythmias sometimes supervene

The white blood cell count can be normal, subnormal, elevated, and even leukemoid in character The spinal fluid usually shows a lymphocytic pleocytosis in the infectious cases Polymorphonuclear cells can be present in the early stages, with transition to a higher percentage of lymphocytes as time passes The level of spinal fluid protein is usually slightly elevated The sugar content is normal, or it may be elevated should the level of blood sugar rise

It is noteworthy that pathologically proved cases have occurred in patients, without headache, fever, stiff neck, or spinal fluid changes Prostration and impairment of consciousness were the key elements here

Treatment

Initial Measures—The adult or child with disturbance in consciousness in an infectious setting should be hospitalized, if possible Isolation precautions are advisable He should be reassured that the physician understands his mental clouding and that his mind will soon become clear again Headache will diminish in intensity with the application of a cool cloth and the administration of aspirin, however, if it persists and is intense, codeine can be given, but in widely spaced doses, to avoid further depression of cerebral function Careful general physical and neurological examinations should be made, and a blood cell count and urinalysis should be done Chest x-ray should be obtained soon after admission, and blood should be drawn for blood culture and for tests of blood urea nitrogen, sugar, calcium, and electrolytes A spinal tap with number 20 or 22 needle should be performed, and opening and closing pressures should be measured Manometric testing by jugular compression should not be done The spinal fluid should be examined immediately for cells and organisms Pandy's test for protein should be made Organisms are sought by (1) staining smears of the centrifuged sediment with gram and acid-fast stains and (2) examining an India-ink preparation for Cryptococcus neoformans Specimens of fluid should be sent to (1) the bacteriology laboratory for culture on routine, tuberculosis, and fungus media, (2) the virus laboratory, for virus isolation, if such service is available, (3) the chemistry laboratory, for determination of sugar, protein, and chlorides, and (4) the serology laboratory, for Wassermann or other serologic test for syphilis

The crucial immediate guide is the color of the fluid and the cell count Xanthochromia of the centrifuged supernatant indicates subarachnoid bleeding rather than encephalitis Pellicle formation indicates extreme protein elevation and is suggestive of tuberculous meningitis or tumor (e g, carcinomatosis or sarcomatosis of the meninges, which can simulate meningo encephalitis) An elevated cell count supports the diagnosis of meningoencephalitis, but the disease can be present without it An electroencephalogram, followed by serial tracings, is valuable when available

General Measures—The patient must be reassured constantly during the procedures and attended closely by the nurses Padded side rails should be put on the bed to prevent the patient from falling and receiving injury during his convulsions If the patient is sufficiently awake to swallow without difficulty, a soft diet should be given, with the patient being spoon-fed if necessary Normal hydration should be maintained It is best not to force fluids in this type of infection because of the danger of worsening cerebral edema The decision to allow the patient to have bathroom privileges or to require his use of the bedside commode or bedpan depends on how drowsy or disturbed the patient is No sedative drugs should be given (unless the patient is hyperexcitable or having convulsions), for they add to the depression of consciousness and, thus, make it difficult to follow the course of the primary brain disease

Most patients with encephalitis do not go beyond the point of drowsiness or lethargy from which they can be aroused, and most of them recover with just the supportive treatment outlined The course of meningo-encephalitis due to mumps is a familiar example These patients have an illness which is indistinguishable from severe "aseptic meningitis syndrome," unless they have sequelae Sequelae are not common after mild encephalitis, though general asthenia may persist for weeks or months When after-effects do occur, they are manifested by defects in mentation, personality, speech, sleep pattern, motor function, hearing, and the ease with which seizures occur[9] Visual impairment is rare, and postencephalitic Parkinsonism has not been commonly reported after any epidemic since that of the "von Economo type," though sporadic cases apparently do occur The arthropod-borne encephalitides and postmeasles encephalitis have a higher incidence of these after-effects than do the others

Management of Severe Cases—In the majority group, therefore, sympathetic supportive management is the key, and the prognosis is good It is in the severe, complicated group that the disease is fearsome and life-threatening Most of the agents that cause the syndrome of aseptic meningitis can produce severe encephalitis The California (Western equine and St Louis type) encephalitis outbreak of 1952 is a recent example of how devastating the illness can be to communities as well as to individuals The treatment of patients with severe encephalitis is one of 'holding the line' and hoping that irreversible brain damage will not occur Supportive measures often permit recovery that would not otherwise take place, but no treatment can save the patient in whom massive destruction of brain tissue has occurred The critically sick patient is stuporous or comatose, respiratory difficulty is dangerously frequent Arterial hypotension and arrhythmias may occur, as may hyperthermia The first problem is to establish the diagnosis with reasonable assurance All other causes of coma have to be considered lest a surgically treatable lesion, a specifically treatable infection, or a metabolic disorder be missed It is valuable to stand back for a moment and consider the reasonable likelihood of trauma (especially subdural hematoma), vascular accident, tumor, brain abscess, metabolic disorder, or drug poisoning Subarachnoid hemorrhage is readily detected by spinal tap Three other conditions which can mimic the spinal fluid findings of encephalitis are (1) partially treated or steroid-masked bacterial meningitis, (2) bacterial endocarditis with small, septic cerebral emboli, and (3) collagen vasculitis Careful systemic appraisal usually clarifies the picture

Hyperexcitability and overactivity should be reduced by an initial dose of 5 cc of paraldehyde given intramuscularly in an adult Grand mal seizures are best suppressed with sodium phenobarbital administered intramuscularly or intravenously Seizures should be suppressed to the point where they neither interfere seriously with respiration nor threaten to exhaust the patient It is inadvisable to give so much drug that the seizures are necessarily obliterated, for this may dangerously add to the depression of vital functions Therefore, the phenobarbital dosage should generally be less than that given to the patient with status epilepticus due to idiopathic epilepsy One may initially administer 130 mg of sodium phenobarbital and then give 30 to 60 mg at intervals sufficient to reduce the frequency of the seizures A dose of 100 mg of diphenylhydantoin (Dilantin) sodium can be given intramuscularly or intravenously every six hours at the same time, this is sometimes helpful in controlling the seizures with use of smaller amounts of phenobarbital

The supportive treatment of the comatose patient begins as soon as possible Airway must be maintained Usually this can be achieved by inserting an oropharyngeal airway and applying nasotracheal suction at frequent intervals If this fails to keep the airway clear, an endotracheal tube must be inserted by the anesthesiologist or a tracheostomy must be performed If the breathing becomes so slowed or shallow that the respiratory minute volume falls below that required for good oxygenation, a respirator should immediately be used One should not wait for cyanosis or severe hypercapnia to develop These are late signs of anoxia and add further to the central nervous system depression It is of note that patients with purely spinal poliomyelitis, with ventilatory insufficiency, can become so obtunded by anoxia and respiratory acidosis that their condition simulates encephalitis They wake up quickly when put in a respirator, which indicates that they did not have true polioencephalitis Asphyxia is all the more dangerous in the patient with an inflamed brain, with its increased oxygen requirement

All fluids and nourishment should be given by the intravenous route The daily salt intake should be restricted to purely replacement amounts so as not to increase cerebral edema When the acute febrile phase is passed, a nasogastric tube can be inserted and tube feedings given by a slow gravity drip If arterial hypotension develops, levarterenol (Levophed) bitartrate or other suitable vasopressor agent should be added to the bottle containing the intravenous solution Arrhythmias should be treated in the usual manner Supraventricular arrhythmias may not show the usual response to vagomimetic measures such as carotid massage because of damage to the brain stem vagal centers The use of an indwelling catheter is necessary if the bladder is distended The patient should be turned from side to side at least every two hours to aid ventilation and drainage of the posterior parts of the lungs and to prevent hypostatic pneumonia

Hyperthermia should be reduced by covering the patient with a sheet kept soaked with cold alcohol and by fans blowing over him The upper part of the body should be kept in a cool oxygen tent A tap water enema at a temperature of 21 C (70 F) may also help

Gluco-corticoids (adrenal steroids), though not of proved value, are said to be useful when the case of encephalitis is obviously severe[10] Use of gluco-corticoids may conceivably reduce brain edema and fever, and it is possible that they might have a favorable influence on the presumably allergic pathogenesis of the postinfectious encephalitides

Miscellaneous Considerations —If the spinal fluid shows large numbers of polymorphonuclear leukocytes per cubic milliliter (300 or more), the patient should always be protected against the possibility of a bacterial meningitis or unencapsulated brain abscess I prefer the combination of penicillin in massive doses, streptomycin, and chloramphenicol (Chloromycetin) in this situation This combination will cover most bacterial pathogens, including the meningococcus The antibiotics are continued unless unequivocal evidence of viral etiology develops, e g, the appearance of the lower motor neuron weakness of spinal poliomyelitis If, as in the usual case, the pleocytosis is mainly lymphocytic, antimicrobials are not indicated, for they are not effective in viral encephalitis except in the rare cases caused by psittacosis or lymphogranuloma virus For these, and in rickettsial infections, one of the tetracyclines should be given

In rare instances, papilledema is found during the acute phase of impairment of consciousness A small number of such patients with encephalitis have improved after a decompression procedure

Occasional patients show the opposite of respiratory depression, namely, hyperventilation There is both hyperpnea and tachypnea, with exhalation of too much carbon dioxide, thus, the partial pressure of carbon dioxide is reduced to dangerous levels Such patients should be put in an oxygen tent and given 95% oxygen and 5% carbon dioxide until the hyperventilation subsides If possible, the blood pH should be closely observed

During the convalescent phase, both the patient and his family need considerable encouragement In addition, physiotherapy is helpful to the patient with residual motor weakness

The long-term outlook for those patients who have required only supportive treatment is generally very good The majority do not develop late mental changes or seizures For those who do, the same supportive and medicinal therapy is required as for persons suffering from idiopathic epilepsy

Prevention

At the present time the only proved preventive measures are (1) poliomyelitis vaccination, for prevention of polioencephalitis and (2) mosquito control, for prevention of the arthropod-borne encephalitides

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THE DEATH OF QUEEN ELIZABETH OF SPAIN—I have reported to Your Serene Highness that the Queen of Spain is pregnant once more Because last year nothing came of her pregnancy, many people have on this occasion cherished doubts likewise Several women have presented her with jewels and given her flower-water to drink in order that she might the sooner conceive and retain what had been vouchsafed to her Others say that in the past year when she miscarried, she, according to the reported custom in France, did not cleanse herself properly that she might again soon become pregnant Be that as it may, Her Majesty hath been weakened mightily by long swoons Some have it that she is half paralysed and cannot use one arm and one thigh as easily as formerly Therefore the leeches hold a grave opinion of her illness, and it has been said that she could not live longer than four or five months These swoons have affected Her Majesty more and more, so that since the Feast of St Michael she has lain mostly abed On the second day of this month the physicians gave her two purgatives and bled her That night Her Majesty, who was very weak, confirmed her former Will, and early in the morning received Extreme Unction They say that the King went to her with frequency and was much affected at her great weakness On that day, about ten o clock in the forenoon, the pains are said to have become very grievous until she gave birth to a young Prince Some assure us that he came alive from the womb of his mother and received baptism others that he was taken from her dead and in pieces, as he could not have been older than five months In order to be exact, it must be said that she is only supposed to have become pregnant in last May when she was with the King in Aranjuez After she had suffered from heavy swooning and great weakness, God Our Lord called her unto Him, about two hours after the birth of the child at noon She is said to have passed away in a most Christian manner May Our Lord God give her eternal peace The King has shown great sorrow on account of this and has withdrawn himself to San Geronimo, the convent outside the city In 1558 we lost here in Spain the Emperor Charles and two Queens In this year '68 we have lost two Princes of Spain and the Queen May God turn His wrath away from this land!—G T Matthews, The Death of Queen Elizabeth of Spain *News and Rumor in Renaissance Europe (The Fugger Newsletters)* 1959

SPECIAL CONTRIBUTION

NEW HEIGHT-WEIGHT TABLES

IMPORTANCE OF NEW CRITERIA

In recent years, considerable emphasis has been placed on the relationship of overweight to mortality and morbidity. There appears to be little doubt that significant overweight is associated with both increased mortality and morbidity. What is significant overweight however, is subject to much individual interpretation. Some of this subjective interpretation is often the result of inadequate therapeutic achievement, and some is often dependent upon the physician's attitude toward his own weight and body image. Obviously, before one can establish a definition of significant overweight, a frame of reference of ideal weight must be established.

For many years now, the medical profession has used a standard of average or desirable weights based on the statistics developed by insurance actuarians. For almost two decades, a chart of "desirable weights" published in the Statistical Bulletin of the Metropolitan Life Insurance Company in 1943 has been the chief standard in use. Recently, these statistics have been revaluated. The findings of the Build and Blood Pressure Study, 1959, of the Society of Actuaries revealed that the new average weight of women was somewhat less than the weights in previous studies, however, the weights of men were increased. The Build and Blood Pressure Study also showed "that the lowest mortality generally occurs among people who are well below average weight."

New tables have been prepared by The Metropolitan Life Insurance Company, these tables are based on weights associated with the lowest mortality, and entitled "Desirable Weights." In general, these weights are somewhat lower than the weights given in earlier tables, but also show a wider range within each frame grouping for the various heights. The latter factor provides the major hurdle in interpretation of these charts, i e, the definition of body frame. Frame is primarily a measurement of bone and should not be a judge of fatness or leanness. Detailed anthropometric measurements of persons are obviously impractical for routine clinical observations. No simple measurements for determination of body frame are available other than knowledge of shoe, glove and hat sizes and these measurements are probably relative to height. At present, estimation of the frame of the body is basically a clinical judgment. Unfortunately, errors in estimation of frame may result in a weight standard that may vary from 6 to 25% from a true standard.

It becomes incumbent upon the physician to pay heed to the newer standards and to constantly maintain a standard of true objectivity. Though there may be adequate reasons for a patient to be maintained at a weight other than his theoretical ideal weight, the medical profession can not afford to disregard the implications of the new standards of weight.

New Weight Tables

Weight in Pounds According to Frame (in Indoor Clothing)

Desirable Weights For Men Aged 25 and Over					Desirable Weights for Women Aged 25 and Over				
Height (with Shoes) 1 inch heels Feet	Inches	Small Frame	Medium Frame	Large Frame	Height (with Shoes) 2 inch heels Feet	Inches	Small Frame	Medium Frame	Large Frame
5	2	112-120	118-129	126-141	4	10	92-98	96-107	104-119
5	3	115-123	121-133	129-144	4	11	94-101	98-110	106-122
5	4	118-126	124-136	132-148	5	0	96-104	101-113	109-125
5	5	121-129	127-139	135-152	5	1	99-107	104-116	112-128
5	6	124-133	130-143	138-156	5	2	102-110	107-119	115-131
5	7	128-137	134-147	142-161	5	3	105-113	110-122	118-134
5	8	132-141	138-152	147-166	5	4	108-116	113-126	121-138
5	9	136-145	142-156	151-170	5	5	111-119	116-130	125-142
5	10	140-150	146-160	155-174	5	6	114-123	120-135	129-146
5	11	144-154	150-165	159-179	5	7	118-127	124-139	133-150
6	0	148-158	154-170	164-184	5	8	122-131	128-143	137-154
6	1	152-162	158-175	168-189	5	9	126-135	132-147	141-158
6	2	156-167	162-180	173-194	5	10	130-140	136-151	145-163
6	3	160-171	167-185	178-199	5	11	134-144	140-155	149-168
6	4	164-175	172-190	182-204	6	0	138-148	144-159	153-173

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* For girls between 18 and 25 subtract 1 pound for each year under 25.

Note. This table was prepared by Metropolitan Life Insurance Company. It was derived primarily from data of the *Build and Blood Pressure Study*, 1959, Society of Actuaries.

Subcommittee on Nutrition,
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PRELIMINARY COMMUNICATION

CLINICAL EXPERIENCE WITH A NEW RAUWOLFIA-FLUMETHIAZIDE PREPARATION

A PRELIMINARY REPORT

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and
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Although the precise nature of the relationship between sodium metabolism and the hypertensive state remains unexplained,[1] the beneficial effects from depleting stores of sodium in patients with hypertension have been recognized for many years Ambard and Beaujard[2] observed more than 50 years prior to the time of writing that salt deprivation reduced the blood pressure in persons with hypertension Although these investigators attributed the effectiveness of their regimen to the restriction of chloride, they were the progenitors of the low-sodium diet as a therapeutic measure in hypertension Some years later, Allen and Sherrill[3] also found that salt restriction was beneficial in patients with hypertension if the sodium-chloride intake was limited to 1 Gm daily, or less In the years which followed, Kempner,[4] Grollman and co-authors,[5] and others[6] reported that a low-sodium diet reduced the blood pressure and decreased the symptoms in patients with hypertension On the other hand, some investigators found that the addition or removal of salt in the diet did not have significant influence on the blood-pressure levels in patients with high blood pressure[6] The variability of response to the low-sodium diet, coupled with its unpalatability, has limited the usefulness of this procedure

A more practical method to attain sodium depletion has been provided by orally effective, potent diuretic drugs which increase the urinary excretion of sodium Chlorothiazide, the first of a number of thiazide compounds to be introduced, possesses specific antihypertensive activity when given alone[7] and potentiates the action of other antihypertensive drugs when administered concomitantly[8] The discovery that other diuretic drugs show similar activity[9] has stimulated their use in combination with older, established antihypertensive drugs

A survey was conducted from April through November, 1959, and the present report concerns our clinical experience with a new diuretic-antihypertensive preparation (Rautrax) Each tablet contains Rauwolfia serpentina, whole root, 50 mg, flumethiazide, 400 mg, and potassium chloride, 400 mg Flumethiazide possesses pharmacological activity similar to that of chlorothiazide, without the development of tolerance, and is free of acute toxicity[10] Potassium chloride has been added for protection against the loss of potassium which may occur during active diuresis

Subjects and Procedures

Subjects—Thirty-seven patients, 35 men and 2 women, were included in this study All patients were ambulant and most were elderly, 26 of the 37 being at least 60 years old The ages for the entire group ranged from 40 to 78 years When first seen, each of the patients received a routine physical examination and appropriate tests to evaluate their cardiovascular state Except for the presence of hypertension, the general physical condition was good in 30 of the 37 patients The remaining seven patients presented evidence of hypertensive cardiovascular disease, with or without kidney disease Previously, six of these seven patients had experienced cerebrovascular accidents, four had histories of congestive heart failure, two had myocardial infarctions, and one patient had severe renal disease Most of the 37 patients were known to have had hypertension for a number of years

Eighteen of the patients had not received antihypertensive therapy prior to administration of the rauwolfia-flumethiazide preparation The other 19 patients had been given one or more of the following medicaments chlorothiazide, reserpine, rauwolfia, and hydralazine hydrochloride

Procedure—All antihypertensive medication was withdrawn from all patients for three or four days During this treatment-free period, blood-pressure levels were recorded The average of several readings was considered to be the control blood pressure for the individual patient Control readings for the entire series ranged from 170/90 to 230/124 mm Hg and averaged 187/101 mm Hg

To facilitate study, the patients were divided into three groups Patients in whom the mean blood pressure (MBP)—the diastolic pressure plus one-

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From the Department of Internal Medicine Scott and White Clinic and the Gulf Colorado and Santa Fe Hospital third of the pulse pressure—was 135 mm Hg or higher were placed in group I Patients with an MBP of from 125 to 135 mm Hg were placed in group II and those with an MBP of less than 125 mm Hg in group III

Medication—The usual initial dosage of the rauwolfia-flumethiazide preparation was 2 tablets a day, however, in a few instances, the patient was started on therapy with 1 tablet daily If the blood pressure was not controlled after several days on the initial schedule, the dosage was increased to 3 or 4 tablets daily, in divided doses The total daily dosage never exceeded 4 tablets Each patient was examined, and blood-pressure levels were recorded, whenever he visited the hospital, at least once a month Six patients required only 1 tablet daily throughout the entire period of observation, while 19 received 2 tablets daily Of the 12 patients who required an increased dosage, 9 finally were receiving 3 tablets daily, and 3 were on daily schedules of 4 tablets At the time this report was prepared, treatment in the 37 patients had been continued for periods of from one to seven months

TABLE 1—*Response to Rauwolfia-Flumethiazide Preparation in Ten Patients in Group I (Patients with Control MBP* of 135 Mm Hg or Higher)*

			Treatment						
					Blood Pressure Mm Hg†				
					Control		Treatment		
Patient No	Age Yr	Sex	Dosage Tablets Day	Period Mo	BP	MBP	BP	MBP	Drop in MBP
1	78	M	2	6	230/124	159	178/100	126	33
2	78	M	1	5	200/115	143	146/84	98	45
3	71	F	2	5	245/109	154	180/90	120	34
4	71	M	2 or 3	5	220/100	140	180/80	113	27
5	70	M	2 or	3	212/120	151	200/100	133	18
6	66	M	2	4	215/115	148	169/97	121	27
7	62	M	2	7	192/107	135	182/104	130	5
8	58	M	4	6	200/113	160	175/95	115	45
9	[illegible]	M	1 or 2	6	186/112	136	210/115	143	−7
10	[illegible]	M	4	7	189/115	139	180/105	130	9

* Mean blood pressure (MBP) is diastolic pressure plus one third of pulse pressure
† Figures given for blood pressure are averages of blood pressure readings recorded for each patient before or during treatment

Other antihypertensive medicaments were not used except that sedatives were added for three persons who were very nervous

Results

Tables 1, 2, and 3 show the responses in the individual patients In every instance, the blood-pressure readings represent the averages obtained before and after treatment

While under treatment, the blood pressure level was lowered in most of the patients in this series For each of the three groups as a whole the average mean blood pressure was at least 10 mm Hg lower after than before treatment, and for the patients in group I, those with the highest pre-treatment blood pressure readings, it was 20 mm Hg lower For the entire series of 37 patients, the blood pressure averaged 163/93 mm Hg after treatment compared with a pre-treatment average of 187/101 mm Hg

With reference to the individual cases (tables 1, 2, and 3), the blood pressure was reduced by treatment in 33 of the 37 patients, reached normal

TABLE 2—*Blood Pressure Response to Rauwolfia-Flumethiazide Preparation in Fourteen Patients in Group II (Patients with Control MBP* of 125 to 135 Mm Hg)*

			Treatment						
					Blood Pressure Mm Hg†				
					Control		Treatment		
Patient No	Age Yr	Sex	Dosage Tablets/Day	Period Mo	BP	MBP	BP	MBP	Drop in MBP
1	77	M	2	6	178/99	125	185/103	130	+5
2	77	M	3	7	195/102	133	174/94	120	10
3	74	M	2	6	176/99	125	143/88	116	21
4	71	M	2	6	180/101	127	161/92	116	11
5	67	M	2	7	186/106	132	160/93	115	17
6	66	M	2 to 4	4	192/101	133	180/98	125	8
7	65	M	2	2	185/96	125	174/89	117	8
8	64	M	3	1	180/107	131	170/100	126	5
9	60	M	2	7	172/102	125	155/95	115	10
10	58	M	2	6	175/110	125	145/90	117	8
11	58	M	1	6	185/99	127	162/82	108	19
12	58	M	2	3	176/100	125	170/103	125	0
13	55	M	2	7	175/100	125	145/90	108	17
14	57	M	1	4	182/97	125	163/95	114	11

* Mean blood pressure (MBP) is diastolic pressure plus one third of pulse pressure
† Figures given for blood pressure are averages of blood pressure readings recorded for each patient before or during treatment

levels (mean blood pressure of 110 mm Hg or less) in 10 of the 33 patients, and near-normal levels (mean blood pressure of 115 mm Hg or less) in an additional 8 of the 33 patients Four patients did not respond to therapy

Thirty-five of the 37 patients did not experience untoward physiological reactions to treatment Of the two patients who did have side-effects one complained of slight gastric irritation, with a sensation of burning in the upper abdomen The other patient experienced a mild sensation of dizziness Withdrawal of the drug was not necessary in either case.

Comment

The experience gained and the observations made during this study lead to the impression that the rauwolfia-flumethiazide preparation used is an effective antihypertensive agent which will lower the blood pressure of patients with hypertension The fact that side-effects were minimal was especially beneficial to the elderly patients who were predominant in this series Perhaps more important was the fact that extreme or sudden drops in the blood pressure—which might have proved disastrous in these elderly patients with arteriosclerosis or cardiac disease—did not occur The combination of three medicaments in one tablet permitted a convenient dosage schedule without the need for other medicaments

Summary and Conclusions

Thirty-seven patients with hypertension were treated with a rauwolfia-flumethiazide preparation (Rautrax) for periods of from one to seven months The dosage was 1 to 4 tablets daily in divided doses, however, 1 or 2 tablets daily usually sufficed The blood pressure was reduced with this treatment in 33 of the 37 patients and decreased to normal or near-normal levels in 18 patients The impression drawn from the results of this study is that the rauwolfia-flumethiazide preparation used is an effective antihypertensive agent which will lower the blood pressure of patients with hypertension

The rauwolfia-flumethiazide preparation used in this study was supplied as Rautrax by E R Squibb & Sons New York 22

Table 3.—Response to Rauwolfia-Flumethiazide Preparation in Thirteen Patients in Group III (Patients with Control MBP of Less Than 125 Mm Hg)*

					Treatment				
					Blood Pressure Mm Hg†				
					Control		Treatment		
Patient No	Age Yr	Sex	Dosage Tablets/Day	Period Mo	BP	MBP	BP	MBP	Drop in MBP
1	7[illegible]	M	1 to 2	[illegible]	180/90	120	142/82	102	18
2	74	M	2	[illegible]	170/90	116	151/89	109	7
3	72	M	2		169/98	121	136/89	104	7
4	65	M	2 to		170/90	116	171/92	118	+2
5	64	M	3		185/90	121	160/90	113	8
6	64	M	3	[illegible]	185/89	121	137/86	103	18
7	62	M	2	[illegible]	155/105	121	148/99	115	6
8	62	M	2		180/94	122	150/87	108	14
9	60	M	1	[illegible]	16[illegible]/9[illegible]	117	160/9[illegible]	116	1
10	[illegible]4	M	2	4	170/94	119	145/86	105	14
11	59	F	2	[illegible]	170/97	12[illegible]	169/95	119	4
12	55	M	3	4	175/98	123	166/97	120	3
13	40	M	2	7	1[illegible]4/99	117	146/97	113	4

* Mean blood pressure (MBP) is diastolic pressure plus one third of pulse pressure
† Figures given for blood pressure are averages of blood pressure readings recorded for each patient before or during treatment

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THE JOURNAL
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WHAT'S IN A NAME?

"What's in a name? That which we call a rose
By any other name would smell as sweet."

SHAKESPEARE was right, of course, that a name is not an intrinsic part of an object, nevertheless, a name is necessary for the object to be identified and essential if the object is to be remembered. We doctors speak or write the names of several hundred drugs masquerading under several thousand trade names. How well do these names enable us to identify the drugs and remember them?

First, let us see how names become attached to drugs. Several different agencies are concerned with names: the Food and Drug Administration, the Convention of the United States Pharmacopeia, the National Formulary Committee, the Council on Drugs of the American Medical Association, and the World Health Organization. The Food and Drug Administration is charged by law with the duty of seeing that the label of the package contains the name recognized in an official compendium, unless the label bears "the common or usual name of the drug, if such there be." The Food and Drug Administration has no power to pass on the suitability of a name (although it can challenge a name if the product renders that name false or misleading). Furthermore, if the drug is new and therefore has not as yet been placed in an official compendium nor possesses a commonly used name, a name that designates its chemical structure may be used instead. These chemical names are usually meaningless to the physician and are almost impossible to remember. For instance, a recent advertisement stated that a certain drug was the *only* (italics theirs) brand of α[(α methyl-3,4-methylenedioxyphenethylamino)-methyl]-protocatechuyl alcohol hydrochloride. Can the practicing physician be expected to recognize, let alone remember, a name that contains 28 syllables, two numerals, and two Greek letters? Then, too, systems of chemical nomenclature differ, one company may designate a drug by one chemical name while another company may use a different chemical name to identify the same drug.

An alternate procedure is for the manufacturer to coin a name which he uses on the label. Since these names are chosen by different manufacturers, the similarity of closely related drugs may be obscured. For instance, Dimetane, which was marked as parabromdylamine maleate, differs only by the substitution of the radical bromine for chlorine from Chlor-Trimeton, which was marketed as chlorprophenpyridamine maleate. The relationship has now been recognized by the inclusion of Dimetane in the National Formulary (NF) as brompheniramine maleate and Chlor-Trimeton in the United States Pharmacopeia (USP) as chlorpheniramine maleate, but in the meantime most physicians have been unaware of the close similarity. A number of other examples are given in an interesting article by Wilson.[1]

Official names are chosen by the USP, but, since new editions appear at five-year intervals, with occasional supplements in between, a drug may be produced and sold for many months before an official name is attached to it. The NF also contains official names. For the most part, the drugs listed in this compendium are analogs of drugs that are listed in the USP or drugs that have been dropped from the USP but are still in use. The National Formulary Committee works closely with the Committee on Revision of the United States Pharmacopeia in an attempt to make the terminology as uniform as possible.

The Council on Drugs of the American Medical Association is concerned with names, in that it accepts a generic name for inclusion in New and Nonofficial Drugs (NND). The very title of the book tells us that the listing of a name therein gives it no official sanction, but, because NND is published yearly, the Council on Drugs is often the first agency to select a "regular" or "generic" name for a new drug. Usually, but not always, this name is later adopted as the official name for inclusion in the USP or NF. The Council on Drugs attempts to obtain the agreement of the manufacturer so that the manufacturer will use the name selected. In most cases the manufacturer is cooperative, sometimes he is not. In the latter event, the Council has no control over the name used except in articles and advertisements which appear in publications of the American Medical Association.

To add to the confusion, the pharmacopeias of other countries may adopt a name for a drug which differs from the one used in our pharmacopeia, although the World Health Organization attempts to bring about some uniformity.

Meanwhile, for most new drugs a trademarked name, popularly called a trade or brand name, has been obtained by the manufacturer or distributor. This name need have no relation to the composition of the drug, it is merely necessary that it be registered with the United States Department of Commerce and that it not resemble too closely a name that has already been registered. As a result of this jumble, the physician tends to use the trade names of drugs as he is confronted with them in advertisements. He thereby exposes himself to hazards of several sorts. Since these names do not give any indication of the chemical formula, the physician has no way of knowing when two trade names designate the same drug. Consultants in the field of infectious diseases have frequently encountered instances in which a physician has changed therapy from an antibiotic with one name to another antibiotic bearing a second name because the patient's illness was not responding to the antibiotic originally given only to find that the first and second antibiotics were actually the same. Furthermore, the physician cannot tell from the trade names whether one drug is a close analog of another and would be expected to have a similar therapeutic effect.

Trade names are chosen to be short, simple, and easy to remember. As an outstanding example, Tao (for triacetyloleandomycin) is a masterpiece of the salesman's ingenuity. Other catchy trade names are Soma, Kynex, Tral, Allbee, and Equanil. Official names, on the contrary, are often long, complex, difficult to pronounce, and consequently hard to remember. Samples of such tongue-twisters which will appear in the forthcoming edition of the United States Pharmacopeia are sulfisoxazole, isoflurophate, phytonadione, ethohexadiol, cetylpyridinium chloride, and prochlorperazine ethanedisulfonate. Small wonder that the practitioner throws up his hands in despair.

Can anything be done about it? I think so. I believe it can be done without changing existing laws and without abdicating any of our cherished rights to make decisions by cooperative action rather than by government fiat. I should like to propose a four-point program. First, the United States Pharmacopeial Convention should establish a list of approved names of drugs. These would be selected before a drug appears on the market and would constitute the official name if the drug is later included in the pharmacopeia. The British Pharmacopeia Commission has already shown that such a system is feasible. It protects itself by stating: "The issue of an approved name does not imply that the substance will necessarily be included in the British Pharmacopeia or that the Commission is prepared to recommend the use of the substance in medicine."

Second, approved names and official names of drugs should be as simple as possible and should be based on a system of nomenclature which would enable the physician to tell by the beginning or ending of the word to which class of compounds the new drug belongs. This has been done for some classes of drugs in the U. S. Pharmacopeia, notably the sulfonamides, the names of which begin with the prefix "sulfa." But it has not been followed in many instances. It would have been helpful, for instance, if all the names of the antibiotics could have ended with the suffix "mycin," but the naming of the first antibiotic "penicillin" and the preemption of the suffix "mycin" for several trade names prevented this. In contrast, the plan adopted for the tetracyclines has worked well. The basic compound is named tetracycline because of its four-ringed structure. The addition of a chlorine radical changes the name to chlortetracycline whereas the addition of a hydroxide radical changes it to oxytetracycline.

When generic names are made available promptly and are simple and meaningful, the third step in the program is to bring them more strikingly and persistently to the practicing physician's attention. Editors of journals should insist that the generic name be used in the title and throughout the body of every article; the trade name could be given in parentheses the first time the drug was referred to in the text or could be stated in a footnote. If editors would require the use of the generic name in every article in a reputable medical journal, the manufacturer would apply to the Pharmacopeial Convention for a name at the same time that he sent his application to the New Drug Division of the Food and Drug Administration. The name would then be available for use in publications as well as on the label.

In advertisements, the generic name should be displayed in type of a size that will command attention—let us say about one-half the size of the type used for the trade name. Of course, this would afford no direct control over the use of generic names in advertisements sent by mail—no direct control, but practitioners of medicine could assert potent indirect control if they would. The pharmaceutical industry is highly responsive to the wishes of the medical profession. If doctors understood that generic names helped them to recognize the therapeutic indications for a drug and that they were, therefore, worth remembering, they could write to the manufacturer whenever an advertisement did not give them the generic name of the drug as well as other information they desired.

The Council on Drugs, representing as it does the informed opinion of the medical profession in this field, has worked closely with the pharmaceutical manufacturers to bring about the early adoption and application of relatively simple, descriptive names for new drugs. They can continue to perform the important task of coordinating information on new drugs and publishing this along with the name adopted by the Pharmacopeia in New and Nonofficial Drugs. This splendid volume, which is revised yearly, should be better known to, and more widely used by, practicing physicians. It contains the up-to-date answers on dozens of questions that come up in everyday practice.

In conclusion, it is evident that the present confusion in nomenclature has just growed like Topsy and has not been the result of deliberate planning on the part of anyone I am quite confident that the majority of pharmaceutical manufacturers are just as anxious as everyone else to see that the doctor's work is simplified, that he is kept promptly and clearly informed, and that his patients are intelligently and effectively treated I hope that all of the many groups and individual persons interested in the proper use of drugs will join forces to bring order to the land before the present confusion becomes chaos "Good order," said Edmund Burke, "is the foundation of all good things"

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WHAT CHIROPRACTIC REALLY IS LIKE[1]

(IN CALIFORNIA, THAT IS)

The cult of chiropractic does not, according to a recent report of the Stanford Research Institute, carry its weight as one of the methods of meeting the health needs of the community Chiropractic is not a "great, uncrowded profession," as chiropractic publicists would have prospective students believe Many of those in practice are doing so poorly that they have to supplement their income by other employment The training that students receive in chiropractic schools is miserable as to faculty, curriculum, and methods, and the number of such students is decreasing as the years pass These facts are included in the findings of this most revealing document

The Stanford Research Institute was engaged in 1958 by the president of the John Randolph Haynes and Dora Haynes Foundation to undertake a study of chiropractic in California This was done as a part of a program of public service engaged in by the Haynes Foundation, according to Mr Francis H Lindley, the president Mr Lindley is an attorney, and his utilization of the Stanford Research Institute to conduct this study with utmost objectivity constitutes a complete avoidance of any charge of medical bias by the chiropractors themselves

The members of the staff of the Stanford Research Institute were successful in obtaining the cooperation of several of the chiropractic organizations in California and of two of the three chiropractic "colleges" They interviewed practicing chiropractors The study also included a sampling of persons interviewed by the California State Department of Public Health in one of their surveys, which was aimed at determination of the manner in which the health needs of the people of that state were being met

Classes in California chiropractic schools are on the lecture basis One school had only two study groups, the advanced class and the freshman class Classes are conducted in the evenings, so that the students may pursue full-time employment, and most of them do Chiropractic school laboratories are unused, and their libraries rarely visited

Chiropractic promoters would have the public believe that they are striving to improve the training of chiropractors to such an extent that only those with some preprofessional college training are admitted to chiropractic schools This has been tried and abandoned by one of the California chiropractic colleges

Chiropractic has been a most unusual American phenomenon Its past history is closely linked to the religious and quasi-religious cults of the 19th century found in northeastern United States It is a product of enterprising "Yankee tradesmen" who have exploited the natural ambition of younger Americans to better their status in life and to condition them to be "martyrs" to medical liberty The exploitation continues in this day of modern medical enlightenment

From time to time The Journal will publish some of the details from this most complete indictment of chiropractic as a claimed valid method of treating the sick State medical societies having problems which involve chiropractic efforts to achieve state licensure and expanded recognition will be able to utilize the facts to show legislatures that this cult is not a worthwhile thing for the health and welfare of the people and that recognition of it certainly is not in their best interests

OEDIPUS AND AKHNATON

The Oedipus legend of Greek mythology is almost three millenniums old For several centuries it was a folk tale, later it was the subject of histrionic art by Aeschylus, Sophocles, and Euripides The legend was preserved during the Middle Ages and rediscovered by Freud as a vital force in his interpretation of psychopathology for the new generation of analysts Velikovsky[1] attributes to Freud the speculation that the Oedipus legend "grew out of the unconscious desire of a son to possess his mother and to dispose of his father by murder From the folklore of primitive peoples, Sir James Frazer gathered together many instances that Freud used to substantiate his theory in the Stone Age the grown up sons of the cave man, the undisputed despot in the cave, usually murdered him in order to possess his wives, their mothers In the neurotic make-up of modern man the Oedipus complex, according to the psychoanalytical theory, plays a prominent role, in the opinion of the analysts the behavior of neurotics and the content of their dreams, as recorded in in numerable medical case histories, support Freud's theory'

King Laius, of pre-Hellenic Thebes, and his wife, Jocasta, were childless for many years When she conceived eventually, the oracle prophesied that the child would kill his father and marry his mother Because of this foreboding, the royal son was abandoned by his parents shortly after birth and cast out of their lives and thoughts The child did not die according to the legend Rather, he was sheltered by shepherds, taken to court at Corinth, and adopted by another royal family The name Oedipus was given him because of his swollen feet (Gr *oidein*—to swell, *pous*—feet) He questioned his adopted parents upon reaching maturity, and, as was the custom in ancient Greece, he sought help from the Oracle at Delphi who told him of his predestined fate Oedipus hoped to avoid such a consequence by leaving his home and wandering incognito throughout the land In his wanderings he met his real father, engaged him in a verbal battle, and later killed him, not far from his native Thebes

The winged Sphinx that guarded the seven gates of Thebes asked of everyone who passed the answer to the riddle of man If the wayfarer failed to solve the riddle, the maiden-monster slew the stranger Oedipus produced the correct answer to the riddle What is it that walks on four legs in the morning, two legs during the day, and three legs at night? Man is a child in the morning, walks upright during the day, and uses a cane in senility The solution to the riddle led the Sphinx to suicide and made Oedipus the hero of Thebes He was given the kingdom, including the recently widowed queen, his mother There are many versions of the story and the events that developed subsequently Upon learning the truth of his nativity, Oedipus blinded himself and left the city in exile, Jocasta killed herself, and the house of Laius fell into decline

The ancient capital of Boeotia in Greece was identified as the seven-gated Thebes to distinguish it from the hundred-gated Thebes in the Luxor valley in Egypt The similarity of name and other items prompted Velikovsky to speculate on the probability that the historical king, Akhnaton of Egyptian Thebes, was the source of the Oedipus legend Akhnaton was the father of king Tutankhamen of the 18th dynasty, synchronous chronologically with the Mycenaean Age of Greece, an era that preceded the Homeric Age Velikovsky has supported his contention with a number of facts and several speculations, deduced from the Egyptologists of whom Howard Carter was the leader Whether or not one accepts the pre-Grecian theory of the Oedipus legend, the tale of Oedipus and Akhnaton is interesting reading for the Egyptologist, the Hellenic historian, the Freudian believer, or the practicing physician

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DYNAMIC ASPECTS OF POSTURE

It is dangerous to limit the freedom of any living organism to adjust itself to changing conditions In particular, the freedom to move about and change position is essential, and to restrict it is to invite serious trouble The mass of evidence on which this conviction is based continues to grow It has been augmented recently by two significant publications

Lillington and his associates[1] used the techniques of bronchospirometry to study the functioning of the right and left lungs separately in five normal men The experiment involved the introduction of a bronchospirometric catheter under fluoroscopic guidance after appropriate medication and the use of oscillometric galvanometers and a photokymograph This made it possible not only to compare the rate of volume flow on right and left sides but also to compare the rates of nitrogen clearance during oxygen-breathing on the two sides in different positions The results confirmed earlier reports that uneven ventilation is present within single lungs, and that changes in position greatly alter the relative functional effectiveness of the two sides

Wood[2] has made clinical observations that reveal the practical significance of Lillington's laboratory experiments Wood's study began with observations of the behavior, during sleep, of a youthful patient with congestive heart failure When turned to lie on his left side, this patient turned over to his right side in 15 to 20 seconds, without waking A longer period on his left side caused dyspnea and coughing These observations led to the discovery of even more serious cases of dyspnea resulting from the assumption of certain positions in various patients and so to the realization that occasional fatalities, particularly in the operating room, may well have resulted from restraining a helpless or unconscious patient in a position capable of causing respiratory distress The conclusion was that, when a patient rolls over to his unfavorable position, the heart sags to that side, obstructs venous return, and further increases any preexisting pulmonary congestion, thereby producing dyspnea The immediate shifting of effusions in various body cavities, the gradual redistribution of edema fluid, and other mechanisms besides may also be involved in particular patients, however, in any case, when conditions are critical, the consequences can be fatal

These findings help to explain the diversity of opinions formerly held on that interesting question On which side should one sleep? It was assumed that there were only four possible positions—prone, supine, right lateral, and left lateral The surprising variety of positions in which healthy children sleep, such as the one with knees and head on the bed and hips in the air, were conveniently ignored in this list of four positions Each of the four had its proponents Each was defended with superficially plausible, sometimes vehement, and generally ill-founded arguments

These arguments were well summarized in a classic article by Johnson and his associates in 1930[3] An essential conclusion from their work was the futility of recommending a particular position for a person to assume when he goes to bed, since any given position is not maintained for long in any case The fact that normal, free people change positions frequently during sleep was clearly brought out This suggested the seriousness of the problem in people who are greatly debilitated by disease, or whose circulation is failing, or whose movements are abolished by casts, bandages, narcotics, intoxicants, or anesthetics

The problem of posture in anesthesia has been reviewed recently by D M Little The importance of adapting the arrangements to the individual case is illustrated by the contrasting situations described by J Abelsohn and by R G Snow and J F Nunn Abelsohn's case is that of a patient who left the operating room in good condition after a pneumonectomy and on being returned to the ward "was placed bolt-upright" In that position she remained unconscious for four hours Within two minutes after being placed flat in bed she was wide awake, recovered from the cerebral ischemia, and was able to converse normally with her husband Snow and Nunn, on the other hand, showed that when a patient comes to the operating room under emergency conditions that preclude the usual emptying of a full stomach, the imminent danger of aspirating gastric contents during the operation can be obviated simply by inducing the anesthesia in a foot-down position This technique, which they describe in detail, has been used in 606 patients and has completely eliminated the aspiration of gastric contents under such conditions

Wood did medicine a service when he reviewed his experiences with the postural aspects of respiration in the Billings Lecture before the Section on Internal Medicine of the American Medical Association in 1959 He also did a service when he introduced the word "trepopnea" to denote a type of dyspnea in which a slight change of position either causes or relieves a respiratory difficulty It is a more inclusive term than "orthopnea," which means a particular type of dyspnea relieved by sitting up "Trepopnea" also has the advantage of emphasizing the fact that posture, especially as it affects respiration, must be thought of not as static but as dynamic

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SURGERY IN THE TREATMENT OF CEREBRAL VASCULAR ACCIDENTS

Increasing success in the surgical treatment of certain kinds of cerebrovascular accidents can be attributed to improved techniques in anesthesiology, intracranial and extracranial vascular surgery, and diagnostic measures such as cerebral angiography

Cerebral angiography has indicated for example that occlusive disease of extracranial arteries is frequently a cause of progressive, intermittent or apoplectic symptoms and signs suggestive of intracranial vascular pathology This alone is an important contribution, for partial occlusion of an extracranial vessel such as the internal carotid artery can usually be treated effectively by endarterectomy[1] Technical developments in small vessel surgery, moreover, suggest that similar methods of treatment for partly occluded intracranial arteries may ultimately be possible as well as intracranial hemorrhagic crises

With respect to subarachnoid hemorrhage, it has become increasingly clear that rupture of an intracranial aneurysm must always be considered In younger individuals an arteriovenous malformation, angioma, or brain tumor must also be thought of, provided trauma, leukemia, and a blood dyscrasia have been ruled out

Angiography should be carried out bilaterally, followed by vertebral angiography if carotid visualization fails to reveal the cause of bleeding Extracerebral angiography, which preferably should include visualization of the aortic arch and the four major extracerebral arteries, can be quite simply and safely done by careful brachial or femoral artery cannulization

Early surgery of ruptured intracranial aneurysms has led to increasingly good results Without surgical intervention the mortality is over 50% Carotid ligation or clamping in the neck is often ineffective and carries a rather high risk of complications On the other hand, direct intracranial surgery with the patient under hypothermia has a mortality of only 15% and in some series much less[2]

Finally, it cannot be too strongly emphasized that every effort should always be made to avoid the diagnosis of cerebrovascular accident or stroke if it is possible to make a more exact diagnosis, such as partial or complete occlusion of a specific vessel at a given site, or intracranial hemorrhage from a specific cause Appropriate and timely medical or surgical therapy can thus be more frequently and more effectively instituted

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CLINICAL NOTES

GUNSHOT WOUNDS OF THE CHEST IN CIVILIAN PRACTICE

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and
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Many excellent reports have been published concerning the care of thoracic wounds during World War II and the Korean conflict, but little has appeared recently about civilian wounds It is the purpose of this paper to set forth the system by which gunshot wounds of the chest are handled at the Marion County General Hospital and to indicate what results may be anticipated

Material

During the period 1948-1957, 83 cases of gunshot wound of the chest were treated on the surgical service of the Marion County General Hospital These cases do not include patients who were dead on arrival or patients who died soon after admission to the emergency ward and were, therefore, never admitted to the surgical service

The cause of wounding was a fight in 31 cases, an attempted suicide in 25, a police action in 19, and an accident in 8 The type of gun was 22 caliber in 19 cases, 32 caliber in 13, 38 caliber in 21, a shotgun in 12, and not listed in 18

Protocol for Management

As soon as the ambulance notifies the hospital that a shock case" is on the way, the surgical resident and other personnel are assembled in the receiving ward Syringes, needles, infusion solutions, oxygen tank, dressings, and other equipment are ready before the patient arrives

When the patient arrives, he is undressed and the wound is inspected If a traumatopnoid ("sucking") wound is present, it is immediately closed with a dressing of gauze and petroleum jelly (Vaseline) The pulse is noted If shock is present or imminent, blood is drawn by an assistant for a type and crossmatch, and an intravenous infusion of saline solution or plasma expander is begun While this is progressing, the surgical resident notes whether there is an adequate airway The chest is examined by inspection and auscultation, and the decision is made whether dyspnea, if present, requires endotracheal aspiration or tracheostomy on the one hand or thoracentesis on the other It is obviously essential to establish an airway and relieve tension pneumothorax or totalatelectasis at once, for shock due to these things will not respond to blood transfusions

The physical examination is now completed, with special attention being given to the missile's trajectory If it is thought that the peritoneal cavity has been involved, exploratory laparotomy is mandatory, unless it is believed that the liver alone has been wounded Chest roentgenograms are obtained, both posteroanterior and lateral views The patient is moved to the x-ray department, if his condition permits, otherwise the roentgenograms are made on a bedside basis Abdominal films are ordered, if indicated

Hemograms made on these patients yielded the following average values hemoglobin concentration 12 2 Gm %, with only 7 patients having levels below 10 Gm %, and white blood cell count 11,840 per cubic millimeter, with 32 patients having above 10,000, 13 above 15,000, and 38 below 10,000 white blood cells per cubic millimeter Thirty-one of the 83 patients were in shock, a finding not reflected by the hemogram Roentgenographic findings on admission were normal in 18 patients and abnormal in 65, 34 had hemothorax alone, 2 had pneumothorax alone, and 29 had both

By this time the patient s condition is fairly well known, and it is possible to decide whether to establish endothoracic drainage by catheter This is done if either substantial pneumothorax or hemothorax recurs after the original needle aspiration or if the needle aspiration is inadequate, i e , if either the lung remains to some extent collapsed or blood or air remains or continues to be withdrawn Thoracotomy is indicated in a patient with massive persistent bleeding or wounding of the heart, great vessels, or esophagus If thoracotomy is not required, the patient is transferred to the ward, where his condition is conscientiously monitored Roentgenograms are always obtained on the next day and again as indicated Antibiotics have been used routinely All patients receive tetanus toxoid or antitoxin

The treatment required in these patients was observation only in 23 (28%), whole blood transfusions in 44 (53%), with 27 (32%) requiring 1,500 cc or more, thoracentesis in 29 (35%), endothoracic catheter with underwater seal in 15 (18%), immediate thoracotomy in 2 (2%), decortication (no patient developed empyema) in 4 (5%), laparotomy in 22 (26%), and administration of streptokinase-streptodornase, with no apparent benefit, in 2 (2%) The average hospital stay was 15 days The longest stay

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From the Department of Surgery Marion County General Hospital in this series was 87 days, and 12 patients were in the hospital over 30 days There were 11 deaths (12%), 8 from abdominal injuries and 3 from thoracic injuries

Summary and Conclusions

Patients with gunshot wounds of the chest must be taken to an emergency ward quickly Once they have arrived where treatment is possible, a carefully designed protocol of management saves further precious moments and insures a maximum salvage rate Antibiotics (usually penicillin and streptomycin) have been routinely given as well as either tetanus antitoxin or tetanus toxoid No complications referable to this practice have been observed, and not a single patient has developed empyema Decortication for hemothorax and captive lung has been necessary in only four cases No endothoracic irrigation of any sort has been employed (Streptokinase-streptodornase was used in two cases without benefit) The axiom that once an airway is established and blood loss treated the primary objective is to achieve complete expansion of the lung in the shortest possible time is substantiated by this series of cases Subsequent to the writing of this report two patients with gunshot wounds of the heart have been successfully treated in this hospital No patient with a gunshot wound of the heart had survived long enough to be included in this study

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ANNULAR PANCREAS

REPORT OF CASE WITH UNUSUAL PRESENTING SYMPTOMS AND CURE

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and
Howard H Hamlin, M D., Chicago

The term "annular pancreas" denotes a condition whereby a part of the pancreas forms a more or less complete ring around the second portion of the duodenum causing obstruction of varying degree This entity was first described by Tiedeman in 1818 The condition is not common, about 88[1] cases are described in the literature in patients ranging in age from 2 days to 74 years[2] The condition may be symptomless, if obstruction is incomplete, and may be found accidentally at autopsy or at surgery when other pathology was suspected It is important to think of this condition when obstruction occurs high in the gastrointestinal tract in children or when vague epigastric symptoms present themselves in an adult

Embryologically the pancreas develops from two sites, the ventral and dorsal anlagen, each with its duct arising from the primitive intestine which later forms the second portion of the duodenum[3] The dorsal anlage grows toward the spleen forming the tail, body, and part of the head of the pancreas The ventral anlage consists of two buds, right and left, the left bud atrophies, and the right ventral bud rotates dorsally and forms the rest of the head of the pancreas Annular pancreas develops when the right ventral anlage becomes adherent to the duodenum and on rotation is stretched, forming a ring,[4] or when the left bud does not atrophy but continues growing, forming the annulus[5]

The pancreatic tissue involved is grossly and microscopically normal pancreatic tissue, but occasionally pancreatitis is seen[6] The annulus may cause from partial to complete obstruction by pressure anywhere and marked dilatation of the first portion of the duodenum At times there is a partial atresia of the duodenum connected with it, which is an important consideration when surgical treatment is instituted

In infants the symptoms are those of duodenal obstruction with projectile vomiting, dehydration, and distention of abdomen There is no bile present in vomitus since this obstruction is above the Vater's papilla[7] Annular pancreas must be distinguished from hypertrophic pyloric stenosis and duodenal atresia The condition does not produce the tumor so often palpated in the epigastrium, and the sausage-like peristaltic movement of the stomach is not apparent Annular pancreas is not found in one sex more than the other Duodenal atresia is a condition which often can only be differentiated at the time of surgery A superior mesenteric artery syndrome has to be considered, but the obstruction is in the first portion of the duodenum In adults the condition may not give any characteristic symptoms unless there is a complete obstruction Why this condition may go on into adult life and not give rise to any symptoms has not been satisfactorily explained,[8] but recurrent bouts of pancreatitis may be the cause for it Without complete obstruction the symptoms are vague epigastric pains without specific radiation and without definite relation to time or type of food intake

Diagnosis is usually made on the basis of roentgenographic findings There is a markedly dilated first portion of duodenum and normal-appearing pylorus There is a smooth concentric narrowing of the second portion of the duodenum without irregularities[9] With air contrast injection a "double bubble sign" is seen, air in the duodenal bulb, none

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From the Department of Surgery, South Shore Hospital Chicago in the descending portion, and air in the third portion again[9]

The treatment is directed toward alleviation of obstruction The ideal course would be the complete excision of the constricting pancreatic ring, but the results obtained were not as good as those obtained through bypass operations The complications of annulus resection are pancreatic fistulas, attacks of pancreatitis, and then recurrence of obstruction, especially if there is an associated partial duodenal atresia[10] In addition the operation puts the patient in a state of shock, and especially in infants it is not well tolerated The bypass operations are the operations of choice Gastrojejunostomy and duodenojejunostomy[11] are the preferred bypass operations More extensive surgery such as gastrectomy and vagotomy do not seem indicated unless there is associated pathology such as peptic ulcer Duodenojejunostomy will give the best result if the duodenal wall has not been thinned out to a great extent This was the surgical procedure in the case presented here, and it provided good emptying of dilated portion of duodenum

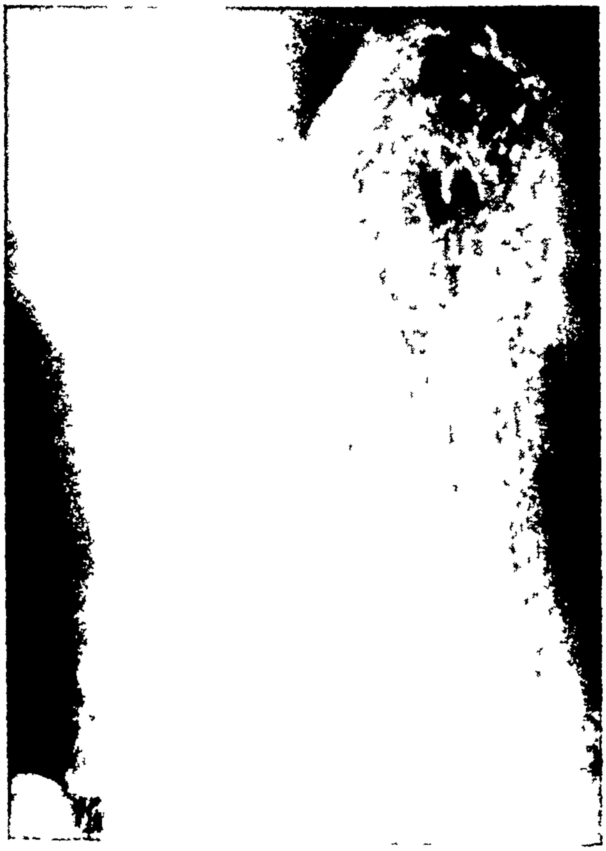

Fig 1—Roentgenogram showing marked dilatation of first portion of duodenum due to obstruction

Report of a Case

A 46-year-old woman was seen in the office with chief complaint of backaches which had persisted for three years and were not relieved by various types of treatments The pain was indefinite in character but was mostly a pressure-like pain in the entire lower dorsal and lumbar area Later on it was elicited that the pain was more to the right of the midline at about the level of D-1 and D-2 to L-1, L-2, or L-3 The patient felt fairly well when getting up in the morning but worse after having been up for awhile and having had something to eat There were no epigastric pains of any kind and no nausea or vomiting, and bowel movements had been normal There was no selective dyspepsia Genitourinary history gave negative findings The patient had no other complaints except nervousness

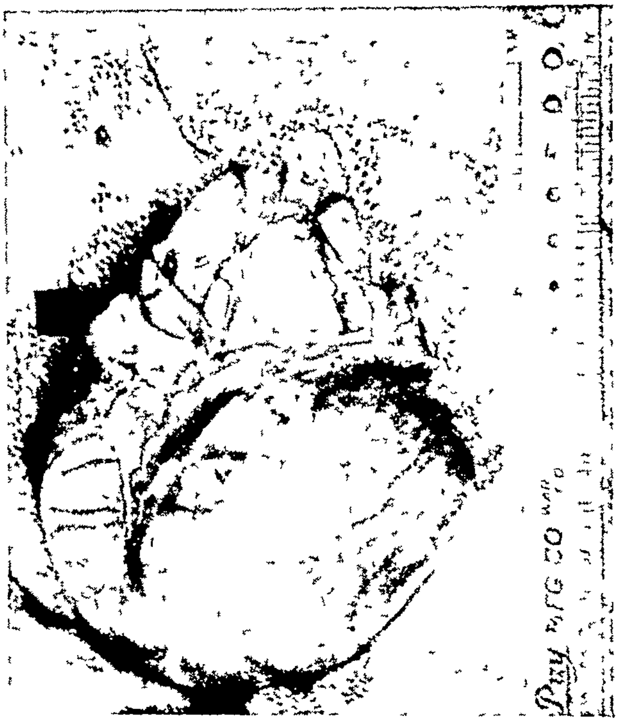

Fig 2—Picture taken at time of surgery, showing marked dilatation of duodenum and pancreatic ring obstructing the second portion

On physical examination the patient did not appear acutely ill, she was tall and lean Examination of head, neck, heart, lungs, and extremities was not remarkable The abdomen was somewhat scaphoid, and there were no localized areas of tenderness Liver and spleen were not palpable There was an increased amount of tympany in the upper part of the abdomen, on palpation a sensation of "fluid slushing around" could be felt over a large part of the right upper part of the abdomen Bowel sounds were normal Examinations of the rectum and vagina did not reveal any abnormality Inspection of the lumbodorsal area revealed a mild kyphosis but no localized tenderness or muscle spasm Because of the increased amount of intravisceral fluid, roentgenograms of the gastrointestinal tract were made which revealed a normal stomach and pyloric region The first portion of the duodenum was markedly dilated, measuring 7 by 10 cm (fig 1) After evacuation the dilated first portion of the duodenum could again be visualized, with barium remaining in it and an outlining the lumen of the duodenum in its enlargement There was no tumor mass seen obstructing the second portion of the duodenum, and there were no irregularities of that portion of the bulb The etiology of the dilatation could not be determined at the time, but annular pancreas, superior mesenteric artery syndrome, and congenital duodenal atresia were considered Because of the marked dilatation, possibly causing the backaches, and subsequent pressure impinging on surrounding structures such as the pancreas and common bile duct, an exploratory laparotomy was recommended to the patient Prior to surgery an intravenous cholangiogram was performed which showed a normally functioning gallbladder and a normal biliary tree which was well visualized

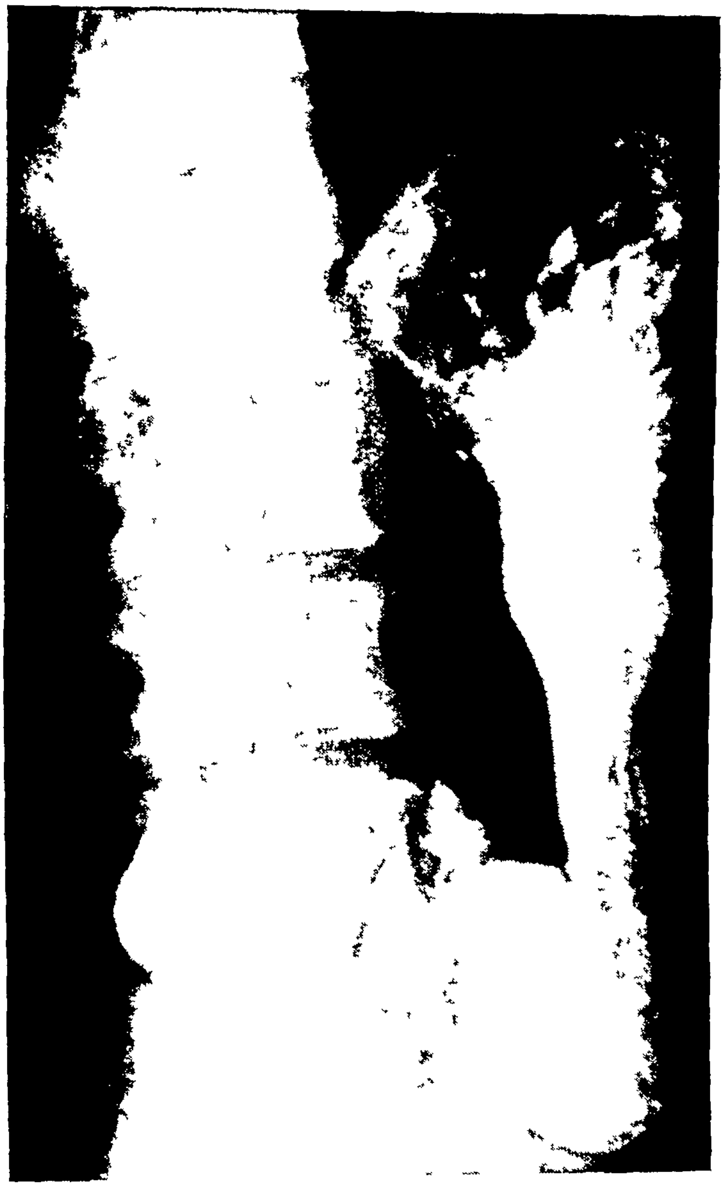

Fig 3—Roentgenogram taken six weeks postoperatively, showing marked decrease in size of first portion of duodenum and functioning duodenojejunostomy

At operation a right upper rectus muscle displacing incision was made and the abdomen entered without difficulty The stomach appeared normal, and the grossly dilated first portion of the duodenum was seen adjacent to a normal pyloric ring (fig 2) Reaching across the middle portion of the second part of the duodenum, gray-yellow lobulated tissue was visualized, almost completely encircling it and causing the obstruction There was also a lesser dilatation distal to the annular pancreas, for which we had no proper explanation The rest of the abdominal contents were normal A posterior duodenojejunostomy was done bypassing the obstruction Postoperatively a Levine tube with suction was used for 24 hours, the patient was given solid foods after 24 hours and made a completely uneventful recovery At the time of this writing, three months after surgery, the patient had remained symptom-free, her backaches had completely disappeared after surgery and had not recurred This indicates that the backache was due to pressure of the enlarged duodenum on the retroperitoneal space and that the bypassing of the obstruction relieved these symptoms Roentgenograms taken six weeks postoperatively (fig 3) show the approximately 90% decrease in the size of the first portion of the duodenum and the bolus going through the anastomosis

Summary

A case of duodenal dilatation caused by annual pancreas occurred in a 45-year-old woman Her chief complaint was backaches, no other symptoms of intra-abdominal origin could be elicited After duodenojejunostomy, complete disappearance of backaches was noted Apparently a complete cure was accomplished by this operation Diagnosis of this rare condition was arrived at by examining the abdomen, finding "slushing around" of fluid in the right side of the upper part of the abdomen, and keeping this rare condition in mind

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CONTAMINATION OF BARIUM ENEMA APPARATUS DURING ITS USE

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An analysis of methods in which barium enemas are performed in some departments of radiology will usually show that complete asepsis is lacking In most, the enema tip is disposable, but the enema set (can, all tubing, glass connecting rods, and tips) is autoclaved or disposed of after each examination in very few, if any, departments

Recently M H Nathan[1] demonstrated sudden rapid increases in rectal pressure, which he interpreted as mass peristalsis He observed that pressures above 75 cm H_2O (55 5 mm Hg) resulted in backflow of fecal matter into the enema container which was suspended at a height of 2 5 ft above the table, this occurred in 12 of 14 patients who exhibited mass peristalsis

It is the purpose of this paper to demonstrate the pressure changes during barium enema examination which may result in contamination of the apparatus and to prevent possible contamination by autoclaving, using a one-way check valve, or using a plastic disposable enema kit

A regular barium enema setup is used except that a y-tube leads off of the rubber tube that goes into the patient Some patients had a bardex tube in the rectum instead of an ordinary rectal tube This y-tube goes to a mercury manometer which contains a floating needle that records pressure changes on a smoked kymographic drum The bottom of the enema can is from 23 to 26 in above the x-ray table

Flow pressure is that pressure in millimeters of mercury above atmospheric pressure at the height of the fluid in the barium enema can while it is flowing Average pressure of barium enema fluid in patient is that pressure millimeter of mercury above atmospheric pressure in the tube after one to three pints of fluid have entered the patient, the flow of barium having stopped

At the previously described height of the barium enema can, the average flow pressure is about 35 mm Hg above atmospheric pressure The patient's average pressure after one to three pints of fluid have entered is about 19 mm Hg (see table)

Twelve separate samples of barium were taken before the barium enema was given, 15 separate samples were taken after the barium enema was used (before each enema the container and tubing were cleansed with hot water and soap) The separate samples of barium in the rubber tubing of different barium enemas were taken at various levels including the level at the bottom of the enema container A sterile needle, syringe, and technique were used The results of the bacteriological cultures were as follows

In 12 cultures of the solution before the barium enema (apparatus having been cleansed with hot water and soap) colonies of yeast-like organisms were present in 12, colonies of diphtheroids were present in 12, and colonies of alpha hemolytic streptococcus were present in 3 In 15 bacteriological cultures in the rubber tubing after the enema colonies of gram negative rods, lactose fermenting and coloform group were present in 7, colonies of diphtheroids were present in 14, colonies of alpha hemolytic streptococcus were present in 7, colonies of yeast-like organisms were present in 12, colonies of Bacillus subtilis were present in 3, colonies of xanthomonas were present in 2, colonies of nonhemolytic streptococcus were present in 1, and colonies of gamma strepticoccus were present in 1

It is apparant that with spasm, mass peristalsis, and/or feeling of evacuation, there is a reflux of fecal barium content into the tubing and barium enema can ascending according to the intensity of spasm Darlow and Bale[2] have shown that any process involving splashing or frothing produces water droplets of bacteria, which remain suspended in the air for variable periods of time Therefore the top of the barium enema container should not be open to air contamination Waisbren, Erlardson, and Fisher[3] have recently written of severe infections caused by mouse virulent strains of Escherichia coli Excreta may contain causative organisms of disease which primarily affect systems other than the gastrointestinal tract such as ova, parasites, hepatitis virus mycobacteria, poliomyelitis[4] and Coxsackie virus

Pressure Reading in Fourteen Patients Taking Barium Enemas (Given in Mm Hg Above Atmospheric Pressure)

Case No	Flow Pressure	Pressure in Patient Av	Pressure During Spasm Mass Peristalsis or Feeling of Evacuation
1	48	16	
2	56	38	
3	56	14	80
4	20	8	
5	30	24	
6	54	16	
7	60	40	80
8	24	12	
9	22	8	
10	50	10	28
11	40	12	43
12	50	10	36
13	50	12	30
14	28	5	20

Summary and Conclusion

Barium enema pressures during spasm were measured Bacteriological cultures were taken at different levels of barium enema tubing including the level at the bottom of the enema container after its use It was found that, according to intensity of

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From the Department of Radiology New York University-Bellevue Medical Center spasm, a reflex of fecal matter can be expected to ascend the barium enema tubing into the barium enema can Autoclaving and/or use of a disposable plastic enema kit to prevent spreading of infection from patient to patient is important A reflux of fecal matter into the tubing and can should be expected depending upon the intensity of spasm that a patient has while receiving a barium enema Accordingly, all types of apparatus for giving enemas should be autoclaved or a plastic disposable enema kit used

303 E 20th St (3)

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SENSITIZATION TO RARE RH ANTIGEN V

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In 1954 a new Rh antigen, designated as V, was reported by DeNatale and others, who, after extensive studies, concluded that the antigen is common in Negroes and rare in white persons "Of 150 West Africans, 40% had V, of New York Negroes 27% had V, of 407 London whites 0 5% had V, and of 444 New York whites 0 5% had V The antigen is inherited as a dominant Mendelian character and belongs to the Rh system The gene V can be part of some cde chromosomes and of some cDe chromosomes, but its precise place in the system is not yet clear "[1]

Report of a Case

A 76-year-old white man was admitted to Lenox Hill Hospital on Oct 12, 1959, for bleeding from the genitourinary tract He gave a history of gastric ulcer and bleeding of long duration, he was operated on for perforated gastric ulcer at Bellevue Hospital at age 43 and underwent three more operations at New York Hospital in 1946 and 1947, where he was given 25 transfusions, without reported reactions On October 14, a unit of blood was requested for transfusion prior to prostatectomy Cross-match of a unit of O, Rh-positive blood was compatible The screening test against Hemantigen gave positive findings, and on testing on Panocel, the antigen involved was found to be V The patient's blood group was O, MN, k, Rh_1rh, The antibody titer was 16 units A sample of his blood was submitted to Dr A S Wiener, who verified the findings and reported the antibody titer to be 12 units by the antiglobulin method and 8 units for ficinated cells The donor's blood was negative for V, and the screening test gave negative findings The patient had no reaction to the transfusion

Comment

The antibody anti-V was encountered in the serum of a patient who had received multiple transfusions in the past As an additional check on our cross-match routine, a screening test on both donor and recipient serums has been added on a panel cell (Hemantigen) which is used routinely in investigation of transfusion reactions and is readily available When a positive reaction is present, we then proceed to the test on Panocel, in order to identify the antigen responsible for the sensitization By this method, it might be possible to demonstrate the presence of unsuspected antibodies, particularly in patients who were receiving repeated transfusions

It is a situation such as in the case reported here, where a white patient probably received blood from a Negro donor and was sensitized, that led to a recent statement that it is dangerous to "mix races" in selecting blood for transfusions On the other hand, it is evident that while on rare occasions, this may constitute some danger, it can be eliminated by careful screening and cross-matching Should a patient be found to be sensitized, compatible blood, even of a rare type, can be found and successfully transfused

Summary

An antibody to a rare antigen (V) was encountered and identified in a patient who had received 25 transfusions (and possibly more) prior to his recent admission A simple screening test has been described as an additional check on compatibility of recipient and donor bloods, which has been adopted in many blood banks

111 E 76th St (28)

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From the Lenox Hill Hospital Blood Bank

ORGANIZATION SECTION

STATEMENT TO SENATE FINANCE COMMITTEE ON H R 12580, 86TH CONGRESS

The problems of the aged and aging have been discussed and debated vigorously during this session of Congress, and considerable controversy has developed as to which of several legislative approaches should be taken to solve them

We are convinced that the approach taken in Title VI, as passed by the House of Representatives, is the proper one But the problems which Congress is setting out to solve are both complex and difficult It is therefore important, we think, to examine them thoroughly before getting down to the specifics of proposed legislative solutions

Despite the fact that old age is relative and based upon physiological changes, the Social Security Act has arbitrarily defined it on the basis of birthdays—65 for a man, 62 for a woman

There are now some 15 5 million Americans over 65 who constitute living evidence that this nation has the finest system of scientific medicine in the world, and that our standards of living are without historic parallel

Each year, our older population will increase, until by 1970 we can expect 20 million people over age 65

The rapid increase in life expectancy has, to some extent, caught us unprepared Our problem as a nation is how best to take advantage of a phenomenon which has brought us a tremendous opportunity to augment America's reservoir of skills, talents and human resources This is not only our opportunity, but our responsibility

Unfortunately, we are not discharging that responsibility at present as well as we could, as well as we should, or as well as we must

For example, our society segregates the aged from employment, and from the community as a whole We retire them from useful work, in too many instances, simply for reasons of chronological age And because we still tend to place undue accent on youth, we all too often thrust older people aside from the mainstream of our day-to day living

We physicians see this at first hand, for in our practice we become uniquely familiar with the process of aging—and with its attrition, its compensations, its inevitability, and its attendant problems No group is more concerned with these problems than the medical profession, nor, in all probability, has any group devoted more study to the aging process or worked harder to find solutions to the many problems which accompany it

The health problems of the aged involve far more than hospitals or doctors' care They involve the older person's other requirements in life, whether these be housing, recreation, community understanding and acceptance, the right to be useful, the courtesy of being treated as individuals, or the opportunity of living as self-reliant, respected members of society

These other requirements of the aged may seem peripheral, but we doctors know that they affect bodily health as directly as a virus For example, suppose we diagnose an illness in an older person, put him in a hospital, and in due course discharge him as cured

If that person cannot find an opportunity to use his skills, talents, and capabilities upon returning to society, if he cannot obtain the emotional support he needs, if he cannot win a place of acceptance within his family, his circle of friends, or his community, it is probable that he will seek, sooner or later, a return to the only shelter available That means the artificial haven of a hospital, a nursing home, or a mental institution

Most older people are, in fact, in good health The diseases to which they are susceptible are no different from the diseases to which people in any age group are susceptible There are no diseases of the aged, but simply diseases among the aged

There is a greater degree of so-called "chronic illness' among older people But the expression is generally misunderstood

The term 'chronic" refers to a recurrent condition, or one that persists over a period of time It does not necessarily imply disability

For instance, a person with impaired hearing, who uses a hearing aid, is chronically ill This does not mean he is either disabled or incapacitated Similarly, a diabetic is chronically ill, although with the help of insulin he can lead a perfectly normal life

The chronically ill are simply impaired Certain medical conditions limit certain of their capacities They are not necessarily disabled

Now I make this point in some detail because our older population is often represented to be sick and debilitated This is not true Let me repeat that most older people are in good health

Dr Ethel Shanas, of the University of Chicago, recently surveyed a representative group of older people with enlightening results She found that 20% or fewer of persons over 65 were sick to degree that illness limited their normal activity

The consensus of those she interviewed seemed to be The way things are now, most people can expect to feel pretty good when they reach 70" I am not suggesting that the aged are as healthy as those in their prime, but I am saying that they are a great deal healthier than they are frequently pictured to be

They would be healthier still if our society would stop shunting them to the sidelines simply because they have achieved an arbitrary number of birthdays

From long experience, doctors have learned that the best defense against sickness is full use by the individual of his physical, mental, and social capabilities And so, we try to keep our patients out of institutions, functioning in society, leading lives as normal as possible

We want them, including our older patients, to remain in the main currents of everyday living When illness sidelines them temporarily in an institution, our aim is to hasten their return to independence and self-sufficiency For the sake of their health, we do not want them to think that there is any emotional bonus in hospitalization, or in long-term residence with the walls of an institution

The financial problems of the aged have also been greatly exaggerated

This Committee, in its consideration of Title VI, should consider these questions

Are the aged as a group too poor to pay for their own medical care?

How many of them are too poor?

To what extent is the cost of medical care the dominant problem of our older population?

In answering the first question, we know that some of the aged are indeed too poor to pay for their own medical care, but the overwhelming majority is not

The bleak economic picture that has been painted of our older people is highly inaccurate Income drops after retirement, true enough But needs are also more modest once the heavy expenses of raising a family are behind

Any assessment of the financial status of the aged must take two facts into account

First, income is not a valid single yardstick for measuring the financial resources of the elderly

Second, the aged are not a homogeneous group from a financial standpoint

Many of our older people have several sources of income Today, nine and one-half million aged receive OASDI benefits, over one million receive veterans pensions, and over one million receive other government pensions such as railroad retirement and civil service Four million are employed, or are the wives of employed persons, one and one-half million receive private pensions, about one million receive annuities individually purchased About half of the aged have some income from assets in the form of interest, dividends, or rent And three-quarters of the aged own liquid assets in one form or another—the highest of any age group

A survey in 1957 by the National Opinion Research Center showed that only 9 6% of those interviewed would be unable to pay a medical bill of $500

And according to reports of the Social Security Administration, almost three out of four beneficiary couples own their own home—87% of them free of mortgage The Bureau found that the median net worth of OASDI recipients, with a wife also entitled to benefits, has increased from $5,110 in 1951 to $9,616 in 1957—an increase of 71% during this six-year period

It is clear from the foregoing that many of the aged are in reasonably good shape economically

It is also clear that future additions to the ranks of our aged will be in even more favorable circumstances For example, today only about 60% of those over 65 are receiving OASDI cash benefits But within a few years, more than 75% will be receiving them

Private pensions are increasing rapidly At present, more than 19 million Americans are covered by private pension plans, with total assets of nearly $40 billion This figure is expected to reach $77 billion by 1965

We can predict a rapid increase in the number of persons eligible to receive veterans pensions We can expect that many more of those reaching 65 in future years will have purchased annuities in preparation for retirement

A few other figures should clinch the point that the aged are not as financially distressed as they are mistakenly reported to be

The median income of aged men increased 50% from 1951 to 1958, whereas that of all men rose only 25%

The tax picture for persons over 65 is substantially better than it is for those under that age

Those over 65 have the lowest indebtedness of any age group, and their financial obligations—for example, to children for educational purposes—are significantly less In many instances, children and relatives of older people become assets rather than financial obligations as the earning capacity changes, and the head of the household status shifts from the father or mother to the children

How does this square, then, with the statistic—which is repeated again and again—that three-fifths of all people 65 and over have less than $1,000 a year of income?

The statistic is accurate, but completely misleading

It would be equally accurate, and just as misleading, to say that in 1957—the most recent year to which that misleading figure applies—63 7% of all Americans had incomes of $1,000 or less per year And nearly 50% of the total of our population over the age of 14 also had annual incomes of under $1,000

Supposing we took as a statistical sample 100 executives who earned $30,000 a year, and their wives If the wives had no private income of their own, we could say of this sample that half of them had incomes of $1,000 a year or less In this particular case their income would, of course, be zero

This is the same statistical technique used to compile the figure cited so often as demonstrative of the financial need of the elderly

It is obvious, Mr Chairman, that such a money income figure is of little or no help in considering the financial problems of the aged If we are to reckon their resources sensibly, we must know how many of the elderly have income from employment, Social Security, pensions, annuities, savings, investments, insurance, or other assets We can measure financial resources intelligently only if we consider them in terms of family income and assets—not individual income alone

And if we want to determine the number of people unable to purchase adequate health care, it is important that we first know how many already receive that care through insurance coverage, from a religious group, a fraternal group, through membership in a union, as ex-seamen, as members of the armed forces, as a matter of professional courtesy, as members of specific religious orders, as veterans entitled to compensation and care, as recipients of help from their families

And it is necessary to consider that 15% of the aged are on public welfare, and therefore eligible to receive medical care under federally aided public assistance programs

The point here is that we should not think that we are dealing with 15½ million hardship cases, for we are not

The fact remains, however, that many people over 65 do have serious financial problems Two and a half million are on Old Age Assistance In addition, we have an undetermined number of people who, while able to finance other costs of living, find it almost impossible to withstand the additional burden of the cost of a serious illness

Even here, things are not as discouraging as they might be, for the percentage of persons over 65 who are needy has been constantly declining In 1950, 22% of all the aged received Old Age Assistance Last year, it had been reduced to 15% and government figures indicate that the figures should drop further—to 11%—by 1970 Thus, the improving economic status of the aged is reflected in a continuing reduction in the numbers of those who are on Old Age Assistance

To sum up, then, any legislation considered by Congress should logically be drafted with two facts in mind

1 That the aged are by and large in good health —with the majority neither sick nor debilitated, and

2 The financial circumstances of the aged are a great deal better than they are often represented to be

I stress these points because they have been overlooked so frequently by those considering the problems of providing health care for the aged

Msgr John O Grady, who is Secretary of the National Conference of Catholic Charities, has spoken wisely on this subject At one of the regional conferences sponsored by the American Medical Association, Msgr O'Grady warned that too many workers in the field of aging are, in effect, not seeing the forest for the trees By concentrating on the small minority of our aged who represent an extreme situation—medically, emotionally, socially, or economically,—they are winding up with a distorted picture, he said In effect, these people have magnified the problems of a minority segment to such an extent that their image of the total group has become blurred They deduce, as a consequence, that most of our older Americans are in poor health, are living on borderline incomes, are substantially less able to contribute to their family or community, are no longer capable producers, and are poised on the brink of bankruptcy or total despair

There is no doubt that Msgr O'Grady is absolutely correct

Unfortunately, a great many Americans seem to have accepted this alarming but distorted evaluation at face value Unaware of the facts, or unmindful of them, these people have yielded to panic and proposed the creation of massive federal machinery to bring about national compulsory health insurance for the aged

Their thinking is, as I have pointed out, based upon the false premises that the aged are, as a group, sick, debilitated, and bankrupt There is another false premise implicit in their thinking This is the mistaken belief that the health care needs of older people can be separated neatly from their other needs

They cannot be Let me repeat that the aged have many and varying needs—in housing, in recreation, in preparation for retirement in winning acceptance and understanding with their communities, in developing new interests, in finding the opportunity to use many of their talents and capabilities which are presently allowed to lie fallow

As an example of how interrelated the needs of the aged can be, a former housing commissioner of the state of New York has estimated that hospital confinement of the elderly could be cut 20% if adequate housing were made available for them

Nonetheless, the country s doctors continue to work to give our older people access to the particular health facilities they may need If this means hospital care, we want hospital beds to be available If this means nursing home care, we want nursing homes to be available If this requires ancillary services, such as homemaker or home care services, we want them to be available

Dr Frederick C Swartz, Chairman of the American Medical Association s Committee on Aging, in his testimony last July before the House Ways and Means Committee, stated

"Care for any segment of our population—the aged included—calls for a cooperative attack on the problem by nurses, doctors, hospitals, social workers, insurance companies, community leaders, and others. It requires flexibility of medical technique.

"In the case of the aged, their health problem primarily involves acute illness and the so-called degenerative diseases. In a very large percentage of cases, the main need is not for an expensive hospital stay or a surgical operation, but for medical care at home or in the doctor's office. In other cases, the important requirement is nursing care in the patient's home, or the home of relatives. And in still others, custodial care in a nursing home or public facility may be the only answer. The point is that the medical needs of this particular segment of the aged are subject to countless variations. . . ."

All legislation which the Congress may consider should take account, in our opinion, of this need for flexibility in meeting the health problems of the aged.

Such legislation should also consider the tremendous and continuing contribution of private citizens, working together on a voluntary basis, to meet the problem. Through cooperation at the community level, retirement villages are now being built in substantial numbers, as are new nursing homes and chronic disease centers. Home care programs are being expanded, recreational facilities are being set up, research programs are getting under way. And new approaches such as progressive patient care, are being used more and more.

In this voluntary effort, the nation's doctors are playing a substantial part. Our A. M. A. Committee on Aging, and similar committees established by all of the state medical societies, have been extremely active in providing leadership and initiative. These committees are working at all levels to meet the health and medical care requirements of older persons. Aging and other committees of medical societies have conducted, and are in the process of conducting, such programs as:

1. Campaigns to correct deficiencies in state and local assistance programs for the needy.

2. Leadership in construction of additional facilities for care of the aged, such as nursing homes. The American Medical Association has cooperated with the American Nursing Home Association in conducting a study of nursing homes. The two Associations jointly developed and approved guides for medical standards in such facilities. These efforts toward higher standards have been simultaneous with continuing liaison with the American Hospital Association and the United States Public Health Service.

3. Promotion of health maintenance programs, including specific campaigns to encourage periodic physical checkups.

4. Stimulation of programs designed to permit the minority of older persons who are ill to remain in the beneficial environment of their homes. These programs include home care, homemaker services, in-the-home rehabilitation and others which substantially reduce the cost of medical care.

We are well aware that there has been a significant increase in the cost of health care in the last 50 years. In fact, the American Medical Association announced in February an initial grant of $100,000 to study all aspects of health care costs, with resulting recommendations that we hope will produce increased efficiency and financial savings. Comparing the medical care of today with that available 50 years ago, however, is like comparing the horse and buggy with the modern automobile.

Physicians individually are also doing what they can to soften medical expenses for those over 65 in modest circumstances. Public welfare, religious and fraternal programs, plus donated services by doctors, provide care for the indigent. And we have proved, again and again, that no person in the United States need go without medical care because he is unable to pay for it.

For the elderly with low family incomes, the A. M. A., in December 1958, called on state medical societies and physicians to expedite the development of low-cost voluntary health insurance and prepayment programs. Physicians were asked to accept reduced compensation for their services, which would make such development possible.

State medical societies and Blue Shield plans immediately responded to the A. M. A.'s request. At present, 40 plans in 37 states are offering non-group coverage to persons over 65, and 24 additional plans in 8 states are completing arrangements for such programs.

I should like to elaborate a little on the subject of private health insurance, for those who favor national compulsory health insurance for the aged state that those over 65 cannot get private health insurance, or that if they can, this insurance is inadequate.

The record disproves this completely. The growth of private health insurance since World War II has been nothing short of phenomenal.

As of Dec. 31, 1943, fewer than 25 million civilians were covered by some form of private health insurance. By 1948, this figure had increased to 61 million. As of the end of 1958, the number of those covered had more than doubled, for 123 million persons—or 71% of the civilian population—had health insurance coverage. By the end of last year, some 127 millions, or 72% of the civilian population, were covered by some form of private health insurance.

Over 100 million people have two or more types of health insurance, and by the end of 1959, some 21 million had major medical expense insurance, a form of coverage only in the experimental stage 10 years ago.

It is significant that the amount of health insurance owned by the aged is growing at the rate faster than that of the population as a whole.

In 1952, only 25% of our older people had health insurance coverage of any kind Today, 49% own some kind of insurance coverage The growth of voluntary health insurance coverage for the group over age 65 is greater, surprisingly enough, than the growth during the same period of voluntary health insurance coverage for all those under 65—100%, as contrasted with only 16%

This rapid increase in coverage of those over 65 can be expected to continue The Health Insurance Association of America estimates that 65% of the aged needing and wanting protection will be insured by the end of this year, and this percentage will increase to 80% by the end of 1965, and to 90% by 1970

To sum up, private health insurance in the United States is well on the way toward accomplishing what the so-called experts in the field of social security have stated on innumerable occasions in the past to be impossible—namely, near-universal coverage of the whole population

Back in 1948, Oscar Ewing, then Federal Security Administrator, reported to President Truman, and I quote, that "at a maximum, only about half of the families in the United States can afford even a moderately comprehensive health insurance plan on a voluntary basis'

Back in 1950, Wilbur Cohen, then of the Social Security Administration staff, testified before the House Ways and Means Committee in favor of the Wagner-Murray-Dingell bills which, at that time, proposed national compulsory health insurance for everyone on the rolls of the Social Security system Mr Cohen declared such action to be necessary because voluntary health insurance obviously could not do the job Therefore, he said, the federal government must take over

But last year, testifying again before the House Ways and Means Committee, Wilbur Cohen admitted on questioning that he had been wrong in 1950 and that voluntary enterprise had done the job He therefore stated that he was not in favor of the extension of national compulsory health insurance below the age of 65

It is significant that Mr Cohen, when asked why voluntary enterprise should not be given an opportunity to do the job for those over the age of 65 as well, replied that he simply did not think it could be done

Hindsight is better than foresight But is it apparent that Oscar Ewing was wrong, and Wilbur Cohen was wrong And it seems clear to me that there are many others who have been wrong when they claim that voluntary efforts and private health insurance cannot meet the problem for the vast majority of our people, the aged included

This brings us to the question of whether or not the health insurance available to the aged is versatile enough, adequate enough, and available enough to meet the need The answer is clearly yes In addition to Blue Cross and Blue Shield, more than 125 private health insurance firms—some of which are licensed to do business in all states—offer coverage to the aged

Benefits are provided in a number of different ways Without exception, older active workers are continued in group insurance plans Most new group plans provide for the continuation of benefits to retiring workers Still other group plans allow the retiring worker to convert his insurance to an individual policy And a number of insurers are now setting up group plans for such associations of older people as Golden Age Clubs

The majority of insurers continue into the later years individual contracts issued at younger ages Those policies especially designed for older people do not require evidence of good health as a condition of eligibility, and after a short probationary period pay benefits for loss due to pre-existing conditions Finally, paid-up-at-age-65 policies are now available

As you can see, Mr Chairman, those who want to buy health insurance have a wide choice of plans, regardless of their age This diversity of coverage is the result of free competition among many insurance companies, all vying with one another in the effort to improve benefits through more efficient methods

Private health insurance and prepayment plans provide the answer to the financing of health care for the vast majority of older Americans They have proved their ability to do the job for those under 65, and, given a chance to continue, without interference, we may confidently expect them to complete the job of providing coverage for the nation's elderly

There is another point which should be stressed Voluntary health insurance today cushions nearly three out of four persons against the financial impact of illness It is logical to presume that those who have had this protection during their working years value it sufficiently to continue their policies after retirement This was not the case, however, with most of the present aged, who did not have health insurance protection during their working years

In other words, in the years ahead, more and more people reaching age 65 will retire with health insurance coverage adequate for their needs

And not only will this coverage be adequate for their needs, but it will represent the free choice of the individual buyer who has been given the opportunity to select the coverage best suited to his particular situation

This is one of the great arguments against national compulsory health insurance for any segment of the population Under our present system, the individual can buy coverage tailored to his own requirements Under several of the alternative plans considered by Congress, this choice of coverage would be eliminated, and in its place would be substituted a rigid, single pattern of benefits which would be imposed on everyone by the government, regardless of his need, regardless of his wishes in the matter

Thus far, Mr Chairman, I have discussed the devices available to the vast majority of the aged for the provision and financing of health care

Now let us consider the needs of the minority, who are either on Old Age Assistance or unable to cope with the cost of serious illness on a budget otherwise adequate for self-support

Sometime ago, the A M A suggested this 8-point program

1 *The Needy Aged* —Here the need is for better organized medical care programs including improved preventive medical care,

2 *The Near-Needy* —If the two and one-half million older persons on old age relief are excluded from the calculation, more than 60% are currently covered by private health insurance The A M A supports a program of federal grants-in-aid to the states for the liberalization of existing OAA programs so that the near-needy can be given health care without having to meet the present rigid requirements for indigency A liberalized definition as determined locally would permit an expanded program and encompass the near-needy group,

3 *Facilities* —Better nursing home facilities for the long-term care of the aged person, especially over the age of 75, are the most urgent health care need before the nation today The average age of nursing home patients is 80, and their average duration of stay is two years It is here that major improvement can be brought about The A M A supports federal programs for the provision of grants through the Hill-Burton mechanism to provide for new nursing home additions to existing hospitals For proprietary nursing homes the A M A supported the recently enacted amendment to the Federal Housing Act providing for government guaranteed mortgage loans to proprietary nursing homes,

4 *Voluntary Health Insurance* —Health insurance and prepayment policies tailored to meet the needs of the aged for long-term nursing home care must be developed as rapidly as possible Health insurers and the Blue Cross-Blue Shield plans across the nation are already experimenting in this new area of coverage,

5 *Home Care* —Care of the aged patient at home is psychologically, medically, and financially superior to institutionalization of any kind Many programs to promote home care are being developed Homemakers' services also provide opportunities for children caring for aged mothers or fathers to continue gainful occupation They need to be expanded,

6 *Attitude Toward Aged* —A basic change in attitude toward the aged person must be brought about The person who reaches 65 should not suddenly be considered non-productive and senescent On the contrary, most persons over 65 are reasonably well and able to work Increased productivity by eliminating compulsory retirement and permitting voluntary change of work is an essential part of the answer to the present problem,

7 *Health Education* —Many older persons are unaware of the need for continuing healthful nutrition and other practices that contribute to good health Above all, the "will to live" is essential to continuing health Preventive medicine measures instituted long before the age of 65 also can contribute materially to the promotion of good health after the age of 65,

8 *The Purchasing Power of the Dollar* —One of the principal economic problems of the aged person in the last twenty years has been the constant and continuing erosion of the purchasing power of his pension benefits A top priority government program to help the aged must be to take measures which are anti-inflationary and maintain the purchasing power of fixed pension and annuity benefits

You will notice, Mr Chairman, that Title VI of H R 12580 is in accord with the principles of that program

This piece of legislation has a great deal to recommend it

1 It is designated to help those who really need help It does not make the mistake of treating our 15½ million older people as a homogeneous group requiring an across-the-board approach By providing aid only to those who need aid, it preserves the right of the non-needy to take care of themselves

2 Title VI, by limiting its effect to the near-needy minority, allows the majority to continue its use of the voluntary method The measure is in no sense compulsory

3 Title VI makes the states primarily responsible for administration of the program—not the federal government We are convinced that the health care costs of the needy and near-needy can best be determined locally, and best be met locally

It is germane to this discussion, I think, to comment on one category of legislation which has been proposed and discussed widely in this Congress The category of which I speak includes all measures which would employ the Social Security mechanism to provide health care for the aged and pay the cost by increasing the Social Security tax

Let me list briefly just some of the objections to this sort of legislative proposal

1 The Social Security approach would cover millions of people who are financing their own health care costs adequately at the present time Whether they need it or not, whether they want it or not, the federal government would cover them

and compel 70 million workers and their employers to pay the bill

2 Under such a system, the federal government would undertake to provide a service purchased from outside sources Instead of cash benefits, it proposes service benefits irrespective of need This is a dangerous precedent, Mr Chairman, which hardly squares with the original purpose of the Social Security Act

3 An approach of this sort would allow the federal government to control disbursement of funds, to decide the benefits to be provided, to set rates of compensation for hospitals, nursing homes, dentists, and physicians, to audit and control government expenditures to hospitals, nursing homes, and patients, and to establish and enforce standards of hospital and medical care Indeed, if the federal government adopted such a measure, it would be compelled to exercise these controls in order to safeguard the taxpayers' money

Could the federal government assume these responsibilities—fiscal and otherwise—without influencing the quality of medical care which it dispensed? The answer is clear it could not

All of these measures disclaim their intention of meddling with the free practice of medicine But if a single government agency were empowered to buy perhaps 10 to 20% of all care in the nations general hospitals, it takes no crystal ball to predict that this agency would wield great power to influence the operation and management of hospitals

It would be well nigh impossible under such a program to avoid a situation in which government employees would be telling doctors what drugs and treatment they could provide, telling the nursing homes what they could and could not do

4 Passage of such a measure would mean overcrowding in our hospitals, which are already hard-pressed to meet the demands for care of our rapidly growing population The overuse of hospitals is predictable, which is borne out in other nations that have experimented with national compulsory health insurance It is human nature for people to seek to collect a benefit for which they have already paid, or for which somebody else is paying

5 As physicians, we believe that patients should be hospitalized or institutionalized only when necessary, and that the length of their stay, as well as the treatment they are given, should be governed by their medical condition The arbitrary limitations imposed by law or the regulations of an administrative agency are not acceptable substitutes for this medical determination

6 The costs of such a proposal are almost impossible to predict But it is safe to say that they would be staggering Social Security taxes are already scheduled to increase sharply in the years ahead To increase them further might well jeopardize the entire Social Security structure through public rebellion

Mr Chairman, it is well to remember that such bills as these are irreversible in nature Once started, they are hard to stop The tendency is to expand them—never to contract them As time went on, the Congress of the United States would face continual pressures for more expanded coverage and more elaborate benefits

7 The passage of such a measure would, therefore, open the way for national compulsory health insurance to cover every man, woman, and child in the country

8 To substitute a compulsory system of health insurance for a voluntary system that has proved its ability to do the job would result in the decline, if not the demise, of private health insurance Those compelled by law to carry the cost of national compulsory health insurance would neither be able nor anxious to carry private health policies as well

This type of legislation would have further bad effects

—It would curb community incentive to support hospitals, for the tendency would be to shift this responsibility from the shoulders of private and local governmental sources to the already overburdened shoulders of the federal government

—It would discourage, at the community level, the freedom to experiment with new techniques, such as home care programs, day hospital service, homemaker services, progressive patient care, and new concepts for treatment through outpatient departments and doctors offices And it is at the community level that such innovations are developed and made to work

—It would discourage families from taking care of their own

—It would restrict beneficiaries in their choice of hospital and physician, for only those physicians, and those hospitals and nursing homes entering into agreements with the federal government, would participate

—The professional relationship between the physician and his patient—the basis of all effective health care—would be severely handicapped Government regulation would be imposed on the physician, and on the patient as well, bringing a third and intruding party between them Required conformance to administrative regulations could also hamper the physician from prescribing treatment which, in his professional opinion, was indicated

—It would discourage the individual approach to patient care, and when this has been disregarded in the past, the result has been mass tragedy rather than mass cure

These, then are some of the reasons why the Social Security approach should not, in our opinion, be invoked

To review briefly the problems that confront the aged their economic status, and the A M A s positive programs for resolving these problems

(1) Today, approximately 60%, or about nine and

one-half million of the fifteen and one-half million persons over 65 are receiving OASDI cash benefits Within a few years, over 75% will receive these benefits,

(2) One and one-half million people now receive cash benefits from private pension plans In the future, a much higher percentage of individuals over 65 will be enjoying such pension benefits, because at the present time, over nineteen million workers are covered by such plans,

(3) A million persons over 65 today receive veterans' pensions, and this number will increase rapidly in future years because of the aging of the veterans' population,

(4) One million others receive railroad or civil service pensions,

(5) Four million individuals are employed, or are wives of employed persons, and their income is relatively the same as the average of other workers,

(6) One million retired persons receive annuities that were privately purchased, and the probability in the future is that many more will have purchased such annuities,

(7) The median net worth of OASDI recipients, with a wife also entitled to benefits, has increased from $5,610 in 1951 to $9,616 in 1957, an increase of 71% during this six-year period,

(8) The median income of aged men increased 50% from 1951 to 1958, whereas that of all men rose only 25%,

(9) Over 70% of aged OASDI beneficiary couples own their own homes, 87% mortgage free,

(10) The liquid assets of persons over 65 are the highest in any age group and have increased the most rapidly,

(11) In 1958, three out of four persons over 65 had liquid assets in some form, 40% had liquid assets over $2,000 in 1958 as contrasted with only 30% in 1949,

(12) The income tax picture for persons over 65 is significantly better than it is for those under that age For example, a married OASDI beneficiary with $4,000 income, including $2,000 from Social Security cash benefits, pays no taxes A person under 65, married, with two children, also earning $4,000, pays approximately $245 federal income tax and $120 Social Security tax, or a total of $365 annual tax on his income,

(13) Those over 65 have the lowest indebtedness of any age group and their financial obligations—for example, to children for educational purposes—are significantly less,

(14) In many instances, children and relatives of older people become assets rather than financial obligations as the earning capacity changes and the head of the household status shifts from the father or mother to the children

There are, of course, many persons over 65 who have serious problems Two and one-half million are now on Old Age Assistance, and an undetermined additional number, although able to finance other costs of living, find it almost impossible to withstand the additional burden of the cost of illness Even here, however, the picture is not discouraging In 1950, 22% of all persons over 65 received Old Age Assistance In 1959, it has been reduced to 15%, and government figures indicate that this percentage should drop to 11% by 1970 Thus, the improving economic status of the aged is reflected in a continuing reduction of those who are on Old Age Assistance

Voluntary health insurance has also shown a remarkably favorable trend for this group In fact, without any government intervention, those over 65 have voluntarily increased their coverage by almost 100% In 1952, only 25% of all the aged were covered Now 49% own some kind of insurance coverage The growth of voluntary health insurance coverage of the group over 65 surprisingly enough is far greater than the growth during the same period of voluntary health insurance coverage for all those under 65—100% as contrasted with only 16%

The American Medical Association recognizes that it is not good enough simply to be against a measure We have opposed, as you are no doubt aware, those legislative proposals which seek to employ the Social Security mechanism as a device for financing national compulsory health insurance for the aged We have given this Committee some of the reasons for our opposition But we have also fulfilled our clear obligation to suggest positive courses leading to the solution of the complex problems facing our older population

We have gone further

We have put into effect programs which have gone far to meet the needs of our senior citizens The medical profession's efforts to achieve the best possible social, spiritual, and medical health of the aged are not new To the contrary, the A M A program represents years of intensive work and study by many councils and committees of the American Medical Association

Let me review that program briefly

1 *Indigents and Near-Indigents* The A M A believes that government agencies, national, state and local, can properly participate in the purchase of or payment for health care provided to indigent persons Our Board of Trustees has stated that the AMA could support "a public assistance program, including federal funds, to cover those citizens who, on the basis of local determination, are considered indigent for the purpose of receiving health care benefits" Our Board of Trustees has concluded that a liberalized public assistance program of this type, designed to aid not only the needy but the near needy, administered by the states, with eligibility and benefits determined locally, is a proper and reasonable government responsibility, supplementing other activities in this area

2 *Facilities* Better facilities for the treatment of long-term disease, especially for aged patients, are needed The A M A supported the FHA amendment providing for government guaranteed mortgage loans for the proprietary nursing home industry The A M A is working closely with the American Hospital Association and other groups to improve the quality of institutional care and to reduce its cost At the same time, the AMA has participated with other organizations in the development of home care programs and homemaker services

3 *Voluntary Health Insurance* The AMA is providing leadership in promoting the expansion of existing prepayment and health insurance plans and the development of new and more effective methods of providing coverage against health care costs of catastrophic nature

4 *Attitude Toward the Aged* A revolution in the nation's attitude toward our older citizens has to occur, if the aged are to take care of themselves rather than become wards of the federal government The most urgent present need is the elimination of mandatory retirement at 65 and discriminatory employment practices against those over 46

Let me repeat the American Medical Association is entirely in favor of helping those who need help But the Association does not believe this necessitates the creation of massive federal machinery to help those who neither need nor want help, and who are capable of handling their own problems at the present time

The question is, who should provide whatever help is needed?

At the Annual Meeting in June of the American Medical Association, the following statement was adopted by our House of Delegates as the policy of the AMA I should like to quote it to you

'Personal medical care is primarily the responsibility of the individual When he is unable to provide this care for himself, the responsibility should properly pass to his family, the community, the county, the state, and only when all these fail, to the federal government, and then only in conjunction with the other levels of government, in the above order The determination of medical need should be made by a physician and the determination of eligibility should be made at the local level with local administration and control The principle of freedom of choice should be preserved The use of tax funds under the above conditions to pay for such care whether through the purchase of health insurance or by direct payment, provided local option is assured, is inherent in this concept "

It is clear that the policy of the American Medical Association is in no way incompatible with the principles upon which Title VI is based

Regrettably, the financing of medical care for the aged has produced violent controversy both in and out of Congress There are two schools of thought

On the one hand are the proponents of OASDI health care amendments, who propose that a radical change be made in what is essentially a cash benefit program Disregarding the fact that such a course can lead only to state medicine, the advocates of this approach call for federal intervention via compulsory Social Security taxation for the financing of medical benefits for all OASDI beneficiaries—regardless of need

This is paternalism at its worst

It would compel the non-needy to accept federal medicine rather than buy medical care voluntarily, through their own resources In fact, the proponents of this plan oppose the right of individuals to pay voluntarily for their own health care They insist that federal government assume this responsibility for everyone eventually—beginning with the aged

This is the outright socialization of the financing of medical care, and we are strongly opposed to it for reasons which we have detailed at some length in this testimony

In contrast to the OASDI approach is the federal grant-in-aid program for the medical care of the near-needy, to be administered locally for locally determined beneficiaries who are eligible This is the method adopted by the House of Representatives by an overwhelming majority It is a method which preserves voluntaryism which permits the non-needy to take care of themselves This follows traditional federal-state organizational structure

It is the economical method, which maintains local autonomy

It is, therefore, the antithesis of centralized, socialized, statist approach of Forand-type proposals

While helping those who need help, it preserves the right of self-reliant individuals to finance their own health care, and bases its approach to the problem on family and community responsibility

This program has been criticized as 'modest"—presumably because its effect would be confined to the needy and near-needy, instead of millions of older people who neither want nor need federal government help

To those critics who call this program modest, we say that fiscal irresponsibility, unpredictable costs, and maximum nationalization are not the accepted criteria for good legislation

We believe that Title VI merits the support of everyone familiar with the problem

We believe that the House Ways and Means Committee is to be commended for its wisdom and statesmanship in developing so sound a proposal

We urge this Committee to accept the carefully considered conclusions of the House, based, as they have been, on months of intensive study

In conclusion, let me repeat that we physicians believe in helping those who need help We have bent our efforts toward providing this help for as long as our profession has existed We are resolute in our determination to continue in this course

MEDICAL NEWS

CALIFORNIA

Pituitary Gland Bank Planned—Establishment of what is reported to be the first pituitary bank was announced July 20 at the University of California Medical Center, San Francisco The chief purpose of the bank is to help assure an increasing supply of human pituitary glands for the treatment of children stunted by a deficiency of growth hormone The cooperation of physicians and the public is being sought in 10 Western States California, Arizona, Colorado, Idaho, Montana, Nevada, Oregon, Utah, Washington, and Wyoming Pituitary bank donations will be arranged in the same manner as donations to eye banks and artery banks Donors will sign an authorization in advance for removal of their pituitaries at death and will be advised to inform their relatives and physicians of this intention

Heart Symposium Planned—The 30th annual Professional Symposium on Heart Disease of the Los Angeles County Heart Association will be held Oct 5-6 at the Beverly Hilton Hotel, Dr Robert W Oblath, chairman, announced Speakers will include Drs Herbert L Abrams, Stanford University, Edward A Edwards, Harvard Medical School, Gordon L Farrell, Western Reserve University, John S LaDue, Sloan-Kettering Institute, Milton Mendlowitz, Mount Sinai Hospital, New York, Eric Neil, Middlesex Hospital Medical School, London, Abraham M Rudolph, Albert Einstein College of Medicine, Maurice B Strauss, Veterans Administration Hospital, Boston, and Albert Sjoerdsma Jr, National Heart Institute, Bethesda, Md Information may be obtained by writing to the Association, 2405 W Eighth St, Los Angeles 57

New Hospital in Long Beach—The 400-bed Memorial Hospital of Long Beach was formally opened June 12 as a voluntary community institution Built at a cost of $10,800,000, the new structure is a part of a city-wide program "for improving and increasing hospital facilities in Long Beach" The hospital is built in the shape of a cross, with the first two floors so located that both have ground-level entrances The central nursing station on each floor is the key to the service core which includes the elevator bank, opening either into the public lobby on one side and the service lobby on the other side Patients will have electrically operated hi-low beds, with a specially designed control panel which permits control of radio, television, nurse intercommunications, and a direct-dial private phone

COLORADO

Faculty Retirements—Dr Alfred H Washburn, clinical professor of pediatrics, and Florian A Cajori, Ph D, professor of biochemistry, retired from the faculty of the University of Colorado School of Medicine, July 1 Dr Washburn, who is also director of the Child Research Council, will relinquish this position to Dr Robert W McCammon, associate clinical professor of pediatrics, Oct 1 Drs Washburn and Cajori have been named professors emeriti

DISTRICT OF COLUMBIA

Dr Shilling Awarded Greek Honor—On June 28, the government of Greece bestowed the Golden Cross of the Order of the Phoenix on Dr Charles W Shilling in a ceremony at Athens, Greece Officials attending the ceremony included the U S Ambassador, the chairman of the Greek Atomic Energy Commission, and members of the Foreign Minister's Office Dr Shilling received this honor for his contributions to the Greek atomic energy program, especially with respect to biomedical matters The citation, signed by Paul the Second, King of the Greeks, was dated last summer and the presentation ceremony awaited Dr Shilling's trip to Europe Dr Shilling joined the staff of the Division of Biology and Medicine, U S Atomic Energy Commission, Washington, D C, in July, 1955

Honors Conferred on Medical Society Officials—The Medical Council of the Washington Metropolitan Area at its meeting June 28 paid tribute to five of its members who had rendered special service to the council Dr Henry P Laughlin, Chevy Chase, Md, president of the council, awarded a special certificate of meritorious service to Dr Theodore Wiprud, who founded the council and who was elected honorary life member and secretary in 1958 Others who received certificates for past service were Dr Ralph M Caulk and Dr James M Moss, Alexandria, Va, past-presidents of the council, and Dr Henry Haskins Ferrell Jr, Alexandria, Va, and Dr William T Joyce, Bethesda, Md, past-vice-presidents The council is made up of the presidents, past-presidents, and presidents-elect of the following medical societies of the Washington Metropolitan Area Alexandria City, Arlington County and Fairfax County (Va) medical societies, Montgomery County and Prince Georges County

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Physicians are invited to send to this department items of news of general interest for example, those relating to society activities, new hospitals, education, and public health Programs should be received at least three weeks before the date of meeting

(Md) medical societies, and the Medical Society of the District of Columbia

ILLINOIS

Hospital Opens Emergency Service Building—Open house in the new $735,000 outpatient and emergency service building at St Francis Hospital, Evanston, was held July 28-29 The one-story structure with basement constructed at the rear of the hospital on the northeast end, houses all the former outpatient facilities plus several new ones and a large emergency service division The outpatient and emergency building is the second step in the $5,630,000 development program at St Francis Hospital, the first was its new food service unit, opened last year

Hospital Honors Staff Members—A recognition dinner for physicians who had served for 25 years or longer on the medical staff of St Francis Hospital, Evanston, was given by the Sisters of St Francis July 14 Included among the 35 doctors, who have given their patients 1,157 years of service since becoming members of the staff, were several who had interned at St Francis Dr Adolph R Konle, Chicago, the second intern to be trained at the hospital and a staff member since 1916, Dr Floyd L McGrath, Evanston, and Dr William L Waner, Skokie, staff members since 1926, Dr Paul J Kullman, Lincolnwood, and Dr Frederick D O'Donnell, Wilmette, on the staff since 1930, and Dr Noel G Shaw, Evanston, a member since 1932

Chicago

Exhibit on Hospitals to Have World Tour—The International College of Surgeons' exhibit, "The Functional Hospital," will remain on display at the Surgery Hall of Fame, 1524 Lake Shore Drive, for the rest of the summer The exhibit, which portrays the "latest in today's and tomorrow's hospital," and was originally installed to celebrate Hospital Month, in May, will leave the Hall of Fame for a world tour in September Its first stop will be the joint meeting of the Canadian and United States sections in Winnipeg, Manitoba, Sept 26-27

Expand Speech and Hearing Clinic Services—The services of the Speech and Hearing Clinic have been expanded as a consequence of the merger of Presbyterian and St Luke's hospitals The clinic is a subdivision of the department of otolaryngology and bronchoesophagology In addition to definitive therapy, the clinic personnel are available for consultation on speech and hearing problems Following an interview, a summary is forwarded to the referring physician For information, write Dr Stanton A Friedberg, Department of Otolaryngology, Presbyterian-St Luke's Hospital, 1753 W Congress Parkway, Chicago 12

Dustfall in Chicago—The lowest average total dustfall ever recorded by Armour Research Foundation for the city of Chicago occurred during June An average 31 9 tons per square mile fell throughout the city The June reading represents an 11% drop from May of this year and a 28% drop compared with June, 1959 Only four collecting stations throughout Chicago showed increases in total dustfall over the month of May three on the South Side and one on the North Side Highest reading for the month was 47 5 tons at a South Side station Lowest reading was registered at a Northwest Side Station

INDIANA

Indiana Blood Banks Organize—The Indiana State Association of Blood Banks, to be affiliated with the American Association of Blood Banks, was organized recently at a meeting in Indianapolis Officers will include Dr John L Arbogast, Indianapolis, president, Dr Jene R Bennett, South Bend, president-elect, and Mr J J Lantz, Vincennes, secretary-treasurer

LOUISIANA

Tulane Appoints New Anatomy Chief—James A Miller Jr, Ph D, has been appointed professor and chairman of the department of anatomy at Tulane School of Medicine, New Orleans He assumes the post formerly held by Dr Harold V Cummins, who retired a year ago and is now assistant dean of admissions Dr Miller received his Ph D degree in zoology from the University of Chicago and has served on the faculties of Ohio University, University of Michigan, and University of Tennessee He has taught at Emory University, Atlanta, Ga, since 1946 In 1959 Dr and Mrs Miller received the annual Research Citation of the Emory chapter of Sigma Xi in recognition of their research on asphyxia of the newborn

Typhoid Outbreak Follows Wedding Reception—The U S Public Health Service in its Weekly Morbidity Report of July 8 announced that the Louisiana State Board of Health supplied information on an outbreak of typhoid fever that followed a wedding reception Thirty cases had been diagnosed among the 80 persons from four parishes who attended the reception Refreshments consisted of home-prepared chicken-salad sandwiches, cake from a commercial bakery, and punch Leftover food was taken home and eaten by at least 17 persons who did not attend the wedding All but 1 of the 30 persons are known to have eaten chicken-salad sandwiches either at the reception or at the home The first laboratory-confirmed case was in a neighboring parish, but 24 others in the parish where the reception was held were being investigated All cultures obtained in this outbreak proved to be Salmonella typhosa, type E-1 Others had serologic evidence of the infection Specimens from a woman who assisted in cooking, boning, and grinding the chicken and mixing the salad were found to be positive for S typhosa, type E-1 This 68-year-old woman denied recent illness, but she gave a history of previous cases of typhoid fever in the family Evidence indicates that she is a chronic carrier, the report stated

MARYLAND

Johns Hopkins Medical School to Increase Size of Classes—The Johns Hopkins University School of Medicine plans to increase the size of its predoctoral program from the present 75 students to 90 beginning in the fall of 1961 Physical facilities, augmented by the completion last year of the new Basic Science Building, will be further increased with present plans calling for the refurbishing of the building housing the departments of anatomy and pathology

Personal—Herbert Bowen Pahl, Ph D, formerly assistant professor of biochemistry at Vanderbilt University School of Medicine, Nashville, Tenn, was appointed executive secretary of the Biochemistry Training Committee, Division of General Medical Sciences, National Institutes of Health, Bethesda He succeeds George M Briggs Jr, who has accepted a professorship with the University of California School of Medicine, Berkeley Dr Pahl will supervise the review by the Biochemistry Training Committee of applications for research training grants in the basic specialties related to biological chemistry ——Dr Frank B Walsh, professor of ophthalmology, Johns Hopkins University, Baltimore, delivered the second University of Toronto Walter W Wright Lecture in Ophthalmology at the Academy of Medicine Oct 23 on "Trauma to the Skull and Certain Ocular Findings" The Walter W Wright Lectureship in Ophthalmology was established a year ago in honor of Dr Walter W Wright, professor emeritus of ophthalmology, University of Toronto

Gift to Help Build Research Building—A gift of $668,000 from the Hoffberger family toward construction of the research building of the Children's Medical Center, Baltimore, was announced July 19 by Mr Walter F Perkins, president of the Johns Hopkins Hospital The Children's Medical Center is a cooperative venture of four medical organizations in the Baltimore area—the Hospital for Consumptives of Maryland (Eudowood Sanitorium), the Robert Garrett Fund for Surgical Treatment of Children, the Harriet Lane Home for Invalid Children, and the Johns Hopkins Hospital The first three of these organizations have established a 9-million-dollar fund to endow the center and have pledged 5 million of the 11 million dollars necessary for its construction Construction is due to start in January, 1961, with completion scheduled for the latter part of 1962 The Hoffberger Research Building will offer opportunities to develop improved diagnostic techniques and treatment for children with heart diseases Other research fields will concern the application of biochemical and biophysical techniques to children's diseases, studies in mental retardation, experimentation in rehabilitation techniques, exploration of the genetic factors in hereditary deformities of children, clinical investigation of respiratory problems, and studies in chronic diseases

MASSACHUSETTS

Appoint Superintendent of Laboratories—Dr Geoffrey Edsall, Washington, D C, was appointed superintendent of the Institute of Laboratories for the Commonwealth of Massachusetts and professor of applied microbiology at the Harvard School of Public Health His appointments were announced by Dr Alfred L Frechette, Boston, commissioner, Massachusetts Department of Health and by Dr John C Snyder, dean of the Faculty of Public Health at Harvard Dr Edsall is director of the Division of Communicable Diseases, Walter Reed Army Institute of Research, and director of the Commission on Immunization, Armed Forces Epidemiological Board Dr Edsall served as director of the Division of Biologic Laboratories in the Massachusetts Department of Public Health from 1942 to 1949 He was assistant professor of public health bacteriology at Harvard from 1947 to 1949 and from 1949 to 1952 was professor of bacteriology at the Boston University School of Medicine He has served as a visiting lecturer on microbiology at the Harvard School of Public Health since 1952 Dr Edsall succeeds Dr Johannes Ipsen Jr as superintendent of laboratories Dr Ipsen resigned, effective July 1, to accept the post of professor of epidemiology and medical statistics at the University of Pennsylvania School of Medicine, Philadelphia

MICHIGAN

Dean Appointed for School of Public Health—Dr Myron E Wegman, secretary-general, Pan American Sanitary Bureau, World Health Organization Regional Office for the Americas, on July 15 was named dean of the School of Public Health at the University of Michigan, Ann Arbor, effective Sept 1 He succeeds Dean Henry F Vaughan, who retired a year ago Dr Wegman, in his present position since 1957, has the major operating and administrative responsibility for coordination of public health activities in 22 Latin American countries The new dean is chairman of the editorial board of the *American Journal of Public Health*, a contributing editor of *Pediatrics* and a member of the editorial board of *Advances in Pediatrics* Dr Wegman has taught in the public health departments of Columbia, Cornell, and Johns Hopkins universities, and in medicine at Yale, the School of Tropical Medicine in Puerto Rico, and at Louisiana State University

NEW YORK

Dr Whipple Wins Kaiser Medal—Dr Edward G Whipple, Rochester, was awarded the 1960 Albert David Kaiser Medal at the annual meeting of the Rochester Academy of Medicine The award is named after the late Dr Albert D Kaiser, a former director of the Monroe County Health Department Dr Whipple is a past-president of the academy and of the county medical society He organized and for several years was chairman of the public health committee of the county society In 1944, he resigned as medical director of the County Welfare Department to act as expert consultant in chest diseases on the Workmen's Compensation Board, a post he held until March last year

Report on Pollen Sampling Network—Sixteen communities will participate this year in the daily pollen sampling network sponsored jointly by the State Health Department and the State Air Pollution Control Board, Dr Herman E Hilleboe, state health commissioner and board chairman, announced July 22 The network will provide daily reports starting Aug 9 and will continue until Sept 29 This is the third year that the network has been in operation during the pollen season in New York State In 1958, the year the network was started, only six stations were set up Last year, 13 stations provided daily reports Dr Hilleboe said that reports from the stations will provide a guide to pollen concentrations in the atmosphere and help hay fever sufferers chart the progress of the hay fever season The sampling stations and pollen counting will be conducted by personnel in local health departments, and other official and voluntary agencies Stations will be set up in Albany, Batavia, Binghamton, Buffalo, Corning, Hornell, Hudson, Ithaca, Melrose, Mineola, Newburgh, Niagara Falls, Troy, Tupper Lake Warsaw, and Yonkers

New York City

Announce Formal Affiliation of Medical Groups—A joint announcement July 8 by Deane W Malott, president of Cornell University, Mr Philip Bastedo, president of the New York Society for the Relief of the Ruptured and Crippled, and Francis Kernan, LL B, president of the Society of the New York Hospital, stated that a new formal affiliation has been signed by the three institutions In effect, this is an affiliation between Cornell University's Medical College, the Hospital for Special Surgery, which is maintained by the New York Society for the Relief of the Ruptured and Crippled, and the New York Hospital, which is maintained by the Society of the New York Hospital The Society of the New York Hospital, created by royal charter in 1771 provides services and facilities for the care and treatment of patients with most types of diseases, for the teaching of physicians and students, and for research The New York Hospital and Cornell University Medical College have worked together since 1910, and in 1927 both institutions entered into an affiliation for the purpose of enlarging cooperation in the advancement of medical care, education, and research Accordingly, new buildings, known as the New York Hospital–Cornell Medical Center, were erected in 1932 The Hospital for Special Surgery, established in 1863, provides services and facilities for the care and treatment of patients suffering from orthopedic, rheumatic, and other crippling conditions It is constructing the Alfred H Caspary Research Building, adjoining the hospital, to provide for its expanding research program Under terms of the new agreement, the Society of the New York Hospital, Cornell University, and the New York Society for the Relief of the Ruptured and Crippled will each continue their independent corporate existences However, cooperative programs have been outlined concerning faculty and hospital appointments

NORTH CAROLINA

Medical Art Project for Facial Prostheses—A pilot study aimed at helping persons disfigured by injury or diseases has been initiated at the Duke University Medical Center The study is being conducted by the center's department of medical art and illustration, with financial support from the Office of Vocational Rehabilitation, U S Department of Health, Education, and Welfare Purpose of the project is to work toward the production of better artificial noses, and other parts of the face This is being done through studying past efforts in this field, consulting with personnel in other medical centers where cosmetic restorations are produced, and experimenting with new materials and techniques Duke Medical Center surgeons and other personnel will cooperate in the project

OHIO

Fellowships Available for Heart Research—The Central Ohio Heart Association announced that men and women with doctor's degrees interested in conducting heart research at Central Ohio institutions have until Sept 15 to apply for fellowships Applicants must hold a doctor's degree from an approved medical or graduate school and have served at least one year of internship or the equivalent Fellowships, both clinical and basic science, will be awarded for one year at an annual stipend of from $2,800 to $8,000 Fellows will be required to spend full time in their research and associated studies A fellow may pursue part-time studies toward a graduate degree An applicant should have a definitely formulated research program in mind to conduct during the tenure of the fellowship and it must be a project of which he is the senior author and is primarily responsible Before applying, he should obtain approval from an established investigator under whom he is to work The Donald Mahanna Fellowship will be awarded to an M D or Ph D who has established himself in research The stipend is $8,000 a year Applicants need not specifically apply for this fellowship Notification of action will be made by Dec 1 for fellowships starting July 1, 1961 Requests for application forms should be directed to the Central Ohio Heart Association, 145 N High St, Columbus 15, Ohio

OKLAHOMA

Physical Examinations Required for Bus Drivers—All Oklahoma public school bus drivers are required to have a medical examination and an opinion as to their physical and mental competency to drive a school bus Examination forms are distributed by the State Department of Education, and the health certificates are to be signed by physicians

Personal—Dr Stewart G Wolf Jr, chairman of the department of medicine and consultant in neurology and psychiatry at the University of Oklahoma School of Medicine, Oklahoma City, was appointed visiting professor of psychosomatic medicine in the University of Cincinnati College of Medicine Dr Wolf made his first of four visits to Cincinnati, Oct 27-28 He returns in December, February, and April ——Dr Robert L Lembke, Pryor, was appointed staff physician in Continental Oil Company's medical division, with headquarters at Ponca City

Alumni Name Executive Secretary—The Alumni Association of the University of Oklahoma School of Medicine announced that an executive secretary has been employed Dr John R Taylor, Kingfisher, alumni president, said the association has employed Mr Lawrence W Rember, 425 N W 44th St, Oklahoma City, for the newly created position For the past 12 years, Mr Hugh Payne, executive vice-president of the Oklahoma Medical Research Foundation, Oklahoma City, has served as volunteer executive secretary He will continue as volunteer consultant Mr Rember served as nationwide field secretary of the American Medical Association for three years and as director of public relations and executive assistant to the general manager for four years He was director of public relations for the American Hospital Association's Blue Cross Plans Commission for the United States and Canada for two years

OREGON

Dr Lewis Awarded Gold-Headed Cane—Dr Howard P Lewis, chairman, department of medicine, University of Oregon Medical School, Portland, was guest speaker at the Gold-Headed Cane Ceremony at graduation exercises of the University of California School of Medicine, San Francisco, June 9 He received the traditional Gold-Headed Cane, modeled after the one carried by John Radcliffe, physician of King William and Queen Mary of England in the early 18th century, and passed on to his successors Dr Lewis will keep the cane, with his name inscribed on it, for a year and then pass it on to the next "distinguished guest speaker"

WEST VIRGINIA

Name Pediatrics Chairman—The appointment of Dr William G Klingberg, of St Louis, as professor and chairman of pediatrics in the School of Medicine of West Virginia Unversity, Morgantown, was announced July 2 Dr Klingberg, who will assume his new duties on Sept 1, is associate professor of pediatrics at Washington University School of Medicine and also a consultant in pediatrics for the universities of Missouri and Illinois In 1957-1958, he was visiting professor in the Ankara (Turkey) University School of Medicine

Personal—Dr Jacob C Huffman, of Buckhannon, was appointed part-time health officer for Upshur County He succeeds Dr Emma Jane Freeman of that city, who was recently appointed director of the division of maternal and child health of the West Virginia State Department of Health She assumed her new duties in Charleston on the first of July —Dr J Howard Anderson, of Welch, a graduate of Washington and Jefferson College, class of 1895, was awarded the honorary degree of doctor of science by his alma mater during the 161st commencement exercises at Washington, Pa, early in June Dr Anderson is a past-president of the West Virginia State Medical Association and was elected in 1956 as West Virginia's "General Practitioner of the Year"

WISCONSIN

Allergy Society Formed—A new organization, the Wisconsin Allergy Society, has been formed, its charter was granted in June The purpose of the Wisconsin Allergy Society is "to promote and encourage the study of allergy and disseminate knowledge pertaining to allergic disease among professional and lay public" The society will conduct its first meeting on Oct 15 in Madison The officers are Drs Harry R Weil, president, Milwaukee, Frederick Kuehl, president-elect, Green

Bay, and John A Aikins, secretary-treasurer, 1212 W Wisconsin Ave, Milwaukee 3

WYOMING

State Poison Control Center—A Poison Control Center, at the Natrona County Memorial Hospital, Casper, is in operation for the State of Wyoming, as a cooperative project of the State Department of Public Health, State Medical Society, and State Pharmaceutical Association The Center, which operates on a 24-hour basis, provides information to physicians about the toxicity of commercial products and drugs so that they may effectively treat poisoning cases The Poison Control Center provides indexing of all toxic materials for the immediate reference of the consulting physician A board-certified pediatrician is on call as a consultant at all times

GENERAL

Stamp Commemorates Employment of Handicapped—A four-cent 'Employ the Handicapped' commemorative stamp will be issued Aug 28 at New York City It will picture a man confined to a wheelchair operating a drill press Issuance of the stamp will coincide with the eighth World Congress of the International Society for the Welfare of Cripples, to be held in New York City under the sponsorship of the President's Committee on Employment of the Physically Handicapped

Request Papers for Psychosomatic Meeting—The American Psychosomatic Society will hold its 18th annual meeting at Chalfonte-Haddon Hall, Atlantic City, April 28-30, 1961 The program committee would like to receive titles and abstracts of papers for consideration for the program Time allotted for presentation of each paper will be 20 minutes The deadline for the submission of abstracts is Dec 1 The program committee requests nine copies of each abstract, which should be addressed to the Chairman, Program Committee at 265 Nassau Road, Roosevelt, N Y

Indian Physician Awarded Rehabilitation Fellowship—The awarding of a Crown Zellerbach Foundation Fellowship in Rehabilitation to Dr Radha Mohan, Mirzapur, India, was announced July 19, by Dr Howard A Rusk, New York City president, World Rehabilitation Fund Dr Mohan began a minimum of one year of postgraduate training in physical medicine and rehabilitation July 1, in the department of physical medicine and rehabilitation, New York University Medical Center Dr Mohan and his wife will also represent India at the eighth World Congress of the International Society for the Welfare of Cripples in New York, Aug 28-Sept 2

International Cerebral Palsy Course—The International Society for the Welfare of Cripples and United Cerebral Palsy, Inc, are sponsoring an international postgraduate course on cerebral palsy in New York City, Sept 6-23 About 30 lecturers will discuss cerebral palsy from a biosocial approach The major categories are "Neurophysiological Basis," "Medical Aspects Motor, Sensory," 'Various Therapeutic Approaches," "Psychological Survey Intellectual, Emotional,' 'Social Needs Private and Public Institutions," 'Education Systems Vocational Exploration," "Recreation," and Research" Visual aids, seminars, and field trips will also be included in the course, which has a $100 tuition fee and is limited to 20 persons For information, write Isabel P Robinault, Ph D, Institute for the Crippled and Disabled, 400 First Ave, New York 10

Prevalence of Poliomyelitis—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated

Area	July 9 1960		July 11 1959
	Paralytic Type	Total Cases	Total
New England States			
Maine			
New Hampshire			
Vermont			
Massachusetts			
Rhode Island	10	12	
Connecticut			
Middle Atlantic States			
New York	2	2	6
New Jersey			2
Pennsylvania	1	1	1
East North Central States			
Ohio			10
Indiana			
Illinois			2
Michigan	1	1	2
Wisconsin			
West North Central States			
Minnesota	1	1	4
Iowa			21
Missouri			9
North Dakota			
South Dakota			
Nebraska			5
Kansas			11
South Atlantic States			
Delaware			
Maryland			
District of Columbia			
Virginia			5
West Virginia	1	1	
North Carolina			4
South Carolina	2	2	2
Georgia			2
Florida	2	2	1
East South Central States			
Kentucky			1
Tennessee	1	1	3
Alabama	1	1	13
Mississippi	1	1	4
West South Central States			
Arkansas	1	1	16
Louisiana	2	4	4
Oklahoma			8
Texas		4	31
Mountain States			
Montana			
Idaho			
Wyoming			
Colorado			1
New Mexico			1
Arizona			2
Utah			
Nevada			
Pacific States			
Washington			1
Oregon			
California	13	15	5
Alaska			
Hawaii			
Territories and Possessions			
Puerto Rico	2	2	
Total	64	4	17

National Medical Association Meets in Pittsburgh – The 65th convention of the National Medical Association will be held at the Penn-Sheraton Hotel, Pittsburgh, Aug 8-11 In addition to the general sessions and the technical and scientific exhibits, there will be section meetings in medicine, surgery, public and rural health, EENT, dermatology, obstetrics-gynecology, radiology, pediatrics, and neuropsychiatry Highlights of the joint scientific sessions will include a panel discussion, Aug 9, on dermatologic therapy The following afternoon, Dr I S Ravdin, John Rhea Barton Professor of Surgery and vice-president in charge of Medical Development of the University of Pennsylvania, Philadelphia, will deliver the Frederick D Stubbs Memorial Lecture A clinicopathologic conference, to be held the afternoon of Aug 10, will be moderated by Dr Douglas Huestis, assistant director of the department of pathology, Western Pennsylvania Hospital Pittsburgh Information may be obtained from Dr John T Givens, 1108 Church St, Norfolk, Va Executive Secretary

Society News –New officers elected for the **American College of Chest Physicians** to hold office during 1960-1961 are president, Dr Mathew Jay Flipse, Miami, Fla, president-elect, Dr Hollis E Johnson, Nashville, Tenn, first-vice-president, Dr John F Briggs, St Paul, Minn, second vice-president, Dr Charles K Petter, Waukegan, Ill, treasurer, Dr Albert H Andrews Jr, Chicago, and assistant treasurer, Dr William E Adams, Chicago The college's 27th annual meeting will be held in New York City, June 22-26, 1961 ——At the 36th annual meeting of the Western Section, **American Urological Association** the following officers were elected president, Dr Charles M Stewart, Los Angeles, secretary-treasurer, Dr John W Dorsey, Long Beach, Calif, and president-elect, Dr James Ownby Jr, San Francisco The 37th annual meeting will be held Feb 6-9, 1961, at the Hotel Sahara, Las Vegas, Nev ——The newly elected officers of the **American Electroencephalographic Society** are as follows president, Dr Jerome K Merlis, Baltimore, president-elect, Charles E Henry, Ph D, Hartford, Conn, secretary, Dr George A Ulett, St Louis, and treasurer, Dr Isadore S Zfass, Richmond, Va

Combined Surgical Meeting in Winnipeg –On Sept 28-29 the United States and Canadian Sections of the International College of Surgeons and the Manitoba Medical Association will hold their annual meetings together in Winnipeg The joint meeting, at the Marlborough Hotel, is being held instead of the usually larger North American Federation meeting because of the scope of the 12th International Congress, held in Rome in May Papers to be presented during the two-day scientific sessions will be on subjects that include jaundice, plastic surgery, cancer of the throat, blood, bone fractures, and diseases of the esophagus General chairman of the meeting is Dr Samuel S Peikoff, Winnipeg, a regent of the college Surgeons from outside of the U S and Canada who will attend include Prof A Mario Dogliotti, of Turin, Italy, president-designate of the International College of Surgeons, Mr Vivian Bartley Green-Armytage, England, Prof José Soler-Roig, Barcelona, Spain, Prof Bernhard Zondek, Jerusalem, and Mr Patrick Wensley Clarkson, England For information, write the International College of Surgeons, 1516 Lake Shore Dr, Chicago 10

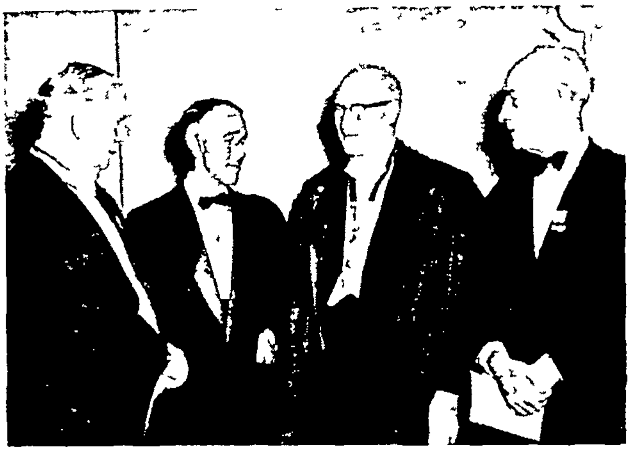
Meeting on Industrial Microbiology –The Society for Industrial Microbiology will sponsor a Conference on *Antimicrobial Agents* at the Mayflower Hotel, Washington, D C, Oct 26-28 The conference is designed to succeed annual antibiotics symposiums conducted for the past seven years In announcing plans for the conference, Dr Charles F Yeager, Chicago, president of the society, said, "It will be required that all papers be submitted in advance and be screened by a well-qualified editorial committee Any interested scientist will be free to submit abstracts and papers for the conference" Program sections will include sessions on "The Mode of Antibiotic Action," "New Anti-Fungal Compounds," "Anti-Tumor and Anti-Virus Compounds," "Clinical Response to Antibiotics," "Isolation and Production of New Antibiotics and Synthetic Production of Natural Antibiotics," "Laboratory Problems of Sensitivity and Resistance of Pathogenic Organisms," and "Chemotherapeutic Substances and Compounds" The conference address is ℅ Society for Industrial Microbiology, 2000 P Street, N W, Washington 16, D C The Society for Industrial Microbiology is a nonprofit organization of scientists employed by colleges and universities, government and public health agencies, and by firms in the food, textile, pharmaceutical, chemical, petroleum, and electronic industries

Society News –The **American Therapeutic Society** has elected the following officers for 1960-1961 president, Dr Harry E Ungerleider, New York City, president-elect, Dr George C Griffith, Los Angeles, vice-president, Dr Adrian Lambert, New York City, Dr Joseph C Edwards, St Louis, and Dr Robert W Oblath, Sherman Oaks, Calif secretary, Dr Oscar B Hunter Jr, Washington, D C, and treasurer, Dr C Raymond Arp, Atlanta, Ga — The officers of the **International College of Surgeons** elected at the international congress in Rome in May are president, Prof Dr A Mario Dogliotti, Turin, Italy (elected previously), president-elect, Dr Lyon H Appleby, Vancouver, Canada, secretary-general, Dr Horace E Turner, Chicago, assistant secretary-general, Dr Arnold S Jackson, Madi son, Wis, and treasurer, Dr Francis L Lederer, Chicago —The following officers were elected at the annual meeting of the American Academy of Tuberculosis Physicians June 11 president, Dr John H Moyer, Philadelphia, first vice-president, Dr Giles Wolverton, Dayton, Ohio, second vice-president, Dr David B Radner, Chicago, officer of sessions, Dr Max Fleishman, Omaha, historian, Dr Kellie N Joseph, Birmingham, Ala, secretary, Dr George P Bailey, Lakewood, Colo, and auditor-editor, Dr Harry J Corper, Denver

Report on Blood Pressures of Men and Women—In its *Statistical Bulletin* for June, the Metropolitan Life Insurance Company reports that new data on blood pressure have recently become available from the investigation, Build and Blood Pressure Study, 1959, made by the Society of Actuaries The data relate to presumably healthy people accepted for life insurance after medical examination More specifically, the figures on average blood pressures in the study apply to men and women accepted for ordinary insurance in the years 1935-1953 The new figures on average systolic and diastolic blood pressures by sex and age indicate that the average for each sex increased steadily with advance in age Among males, the averages for systolic pressure rose steadily from 117 mm at ages 15-19 to 132 mm at ages 60-64 The averages for diastolic pressure rose from 71 mm to 80 mm, but more slowly after age 30 than before Among women, the average systolic blood pressure increased from 114 to 134 mm and the diastolic from 70 to 81 mm The averages for women increased more gradually than those for men at the younger ages, but more rapidly than those for men past age 40 The average blood pressures were somewhat higher for men than for women up to age 45, the maximum difference being 4 mm in systolic pressure—at ages 20 34 years—and 2 mm in diastolic pressure—at ages 25-44 The averages were identical for the two sexes at ages 45 54, but were slightly higher for women than for men at ages 55 and over The new study also shows the relation between weight and blood pressure among persons accepted for ordinary insurance There was a fairly systematic rise in average blood pressures with increase in body weight At ages 40-49 the average systolic blood pressure for medium-height men weighing 195 to 214 lbs was 5 mm higher than for those weighing 115 to 134 lbs

CANADA

Canadian Medical Association Meeting—On June 13, the 93rd annual meeting of the Canadian Medical Association was held in Banff, Alberta One of the highlights of the scientific program was the Osler Oration, an endowed lectureship of the C M A which honors the memory of the distinguished Canadian physician, Sir William Osler Sir Russell Brain, of London, England, gave the 10th oration, June 16, presenting, "Osler and Medicine Today" On June 15, Dr R M Parsons, of Red Deer, Alberta, was installed as president of the Canadian Medical Association, succeeding H R H The Duke of Edinburgh



Four physicians, representing England, Canada, Scotland, and the United States, are shown together prior to the general meeting of the Canadian Medical Association Shown (l r) are Sir Russell Brain, London, England, Dr L Henry Garland, San Francisco, delegate from the American Medical Association, Dr E Kirk Lyon, deputy to H R H The Duke of Edinburgh, president of the C M A, and Dr Edward R C Walker, Edinburgh, official delegate from the British Medical Association

FOREIGN

Pakistan Seeks Medical Speakers—The Pakistan Medical Association is inviting representatives from the member nations of the World Medical Association to present papers at the sixth All Pakistan Medical Conference in November in Karachi Physicians wishing to attend the meeting should communicate with Dr N A Ansari, Secretary of the Sixth All Pakistan Conference, PMA House, Garden Road, Karachi 3, Pakistan

New Site for Medical Photography Congress—The first International Congress on Medical Photography and Cinematography, originally to be held in Cologne, will be held in Dusseldorf, Germany, Sept 27-30, at the Exhibition Ground The site has been changed because of the large number of registrants for the congress, which will combine lectures and film demonstrations with an exhibition of scientific photographs and apparatus For information, write Deutsche Gesellschaft fur Photographie e V, 1st International Congress on Medical Photography and Cinematography, Koln, Neumarkt 49, Germany

CORRECTION

Open Intracardiac Operations.—In the contribution entitled "Postoperative Care After Whole-Body Perfusion and Open Intracardiac Operations," by Drs Lyons, DuShane, and Kirklin, appearing in The Journal, June 11, page 625, an error appeared with regard to the given name of one of the authors The name was given as James W Kirklin, M D It should be John W Kirklin, M D

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC

Educational Council for Foreign Medical Graduates Stations around the world Sept 21, 1960 Exec Director, Dr Dean F Smiley, 1710 Orrington Ave, Evanston, Ill

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners Part I, Various Cities, Sept 7-8 Part II Applications must be received at least six weeks before the date of the examination Exec Sec, Dr John P Hubbard, 133 South 36th St, Philadelphia

BOARDS OF MEDICAL EXAMINERS

Alabama *Examination* Montgomery, June 20-21 *Reciprocity* Continuously Sec, Dr D G Gill, State Office Bldg, Montgomery 4

Arkansas * *Examination and Reciprocity* Little Rock, Nov 10-11 Sec, Dr Joe Verser, Harrisburg

Alaska * On application in Anchorage or Fairbanks Sec, Dr W M Whitehead, 172 South Franklin St, Juneau

California *Written* Los Angeles, Aug 22-25 and Sacramento, Oct 17-20 *Oral and Clinical* Los Angeles, Aug 21, and Los Angeles, Nov 29 *Oral for Reciprocity Applicants* San Francisco, June 18, Los Angeles, Aug 20 and Nov 19 Sec, Dr Louis E Jones, Room 536, 1020 N Street, Sacramento

Canal Zone On Application Acting Sec, Dr B K Levin, Health Bureau, Balboa Heights

Colorado * *Examination* Denver, Dec 13-14 Exec Sec, Miss Mary M McConnell, 715 Republic Bldg, Denver 2

District of Columbia * *Examination* Washington, Dec 12-13 *Reciprocity and Endorsement* Continuously Deputy Director, Department of Occupations and Professions, Mr Paul Foley, 1740 Massachusetts Ave N W, Washington 6

Florida * *Examination* Miami Beach, Nov 20-22 *No Reciprocity* Sec, Dr Homer L Pearson, 901 N W 17th St, Miami 36

Guam *Subject to Call* Sec, Dr F L Conklin, Agana

Maryland *Examination* Baltimore, June 13-16 (Tentative) Sec, Dr Frank K Morris, 1211 Cathedral St, Baltimore 1

Minnesota * *Examination* Minneapolis, Oct 18-20 *Reciprocity* November Sec, Dr J P Medelman, 230 Lowry Medical Arts Bldg, St Paul 2

Montana *Examination and Reciprocity* Helena, Oct 4 Sec, Dr Thomas L Hawkins, 555 Fuller Ave, Helena

Nebraska * *Examination* Omaha, June Director, Bureau of Examining Boards, Mr R K Kirkman, Room 1009, State Capitol Bldg, Lincoln 9

Nevada *Examination and Reciprocity* Reno, Sept 7 and Dec 7 Sec, Dr G H Ross, 112 North Curry St, Carson City

New Hampshire *Examination and Reciprocity* Concord, Sept 14-17 Sec, Dr Edward W Colby, 61 South Spring St, Concord

New Jersey *Examination* Trenton, Oct 18-21 *Reciprocity* Continuously Sec, Dr Royal A Schaaf, 28 West State St, Trenton

New Mexico * *Examination and Reciprocity* Santa Fe, Nov 21-22 Sec, Dr R C Derbyshire, 227 East Palace Ave, Santa Fe.

Ohio *Examination* Columbus, Dec 12-14 *Endorsement* Columbus, Aug 12 and Oct 4 Sec, Dr H M Platter, 21 W Broad St, Columbus 15

Oklahoma * *Endorsement* Oklahoma City, Sept 25 Exec Sec, Mrs E L Haidek, 580 Home State Life Bldg, Oklahoma City

Puerto Rico *Examination* San Juan, Sept 6-10 Sec, Dr Herminio Mendez Herrera, Box 9156, Santurce

Rhode Island * *Examination* Providence, Oct 6 7 Administrator, Division of Professional Regulation, Mr Thomas B Casey, 366 State Office Bldg, Providence

South Dakota * *Reciprocity* Continuously Exec Sec, Mr John C Foster, 300 First National Bank Bldg, Sioux Falls

Texas * *Examination* Fort Worth, Dec 1-3 *Reciprocity* Fort Worth, Aug 20 and Dec 1-3 Sec, Dr M H Crabb, 1714 Medical Arts Bldg, Fort Worth

Washington * *Reciprocity* Continuously Administration, Mr Thomas A Carter, Capitol Bldg, Olympia

Wyoming *Written* Cheyenne, Oct 3 *Oral for Reciprocity Applicants* Cheyenne, Oct 3 Sec, Dr James W Sampson, State Office Bldg, Cheyenne

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arizona *Examination* Tucson, Sept 20 *Reciprocity* Tucson, Sept 30 Sec, Mr Millard G Seeley, University of Arizona, Tucson

Arkansas *Examination* Little Rock, Oct 20-21 *Reciprocity* Continuously Sec, Dr A W Ford, Education Bldg, Little Rock

Colorado *Examination and Reciprocity* Denver, Sept 7-8 and Dec 7-8 Sec, Dr Esther B Starks, 1459 Ogden St, Denver 18

Connecticut *Examination* New Haven, Oct 8 *Reciprocity* Continuously Exec Asst, Mrs Regina G Brown, 258 Bradley St, New Haven 10

District of Columbia *Examination* Washington, Nov 21-22 Deputy Director, Department of Occupations and Professions, Mr Paul Foley, 1740 Massachusetts Ave N W, Washington 6

Florida *Examination* Miami, Nov 5 *No Reciprocity* Sec, Mr M W Emmel, Box 340, University of Florida, Gainesville

Kansas *Examination* Pittsburg, Nov 4-5 *Reciprocity* Continuously Sec, Dr Leon C Heckert, Kansas State College, Pittsburg

Michigan *Examination* Ann Arbor and Detroit, Oct 14 15 Sec, Mrs Anne Baker, 116 Stevens T Mason Bldg, Lansing

Minnesota *Examination* Minneapolis, Oct 4-5 Sec, Dr Raymond N Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14

Nebraska *Examination* Omaha, June Director, Bureau of Examining Boards, Mr R K Kirkman, Room 1009, State Capitol Bldg, Lincoln 9

Oklahoma *Examination* Oklahoma City, Sept 23-24 Exec Sec, Mrs L Haidek, Braniff Bldg, Oklahoma City

Oregon *Examination* Portland, Sept 10 *Reciprocity* Continuously Sec, Dr Earl M Pallett, Box 5175, Eugene

South Dakota *Examination* Vermillion, Dec 2-3 *Reciprocity* Continuously Sec, Dr Gregg M Evans, Custer

Wisconsin *Examination* Madison, Sept 9 Milwaukee, Dec 10 Sec, Dr W H Barber, 621 Ransom St, Ripon

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*Basic Science Certificate required

DEATHS

Andersen, Norbert Ⓜ Jamaica, N Y, Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin, Prussia, Germany, 1923, died in the Forest Hills (N Y) General Hospital May 18, aged 66, of heart failure

Argue, Forrest Birkley Ⓜ Pittsfield, N H, McGill University Faculty of Medicine, Montreal, Que, Canada, 1924, member of the staff of the Concord (N H) Hospital, died May 7, aged 62, of coronary occlusion

Aronson, Sam John Rosenberg, Amarillo, Texas, University of Texas School of Medicine, Galveston, 1926, member of the American Academy of General Practice, served as county health officer, veteran of World War II, affiliated with the Northwest Texas Hospital and the St Anthony's Hospital, where he died May 6, aged 57, of cerebral vascular accident

Baird, Albert Clark, Parsons, Kan, Eclectic Medical College, Cincinnati, 1927, veteran of World War II, died in St Francis Hospital, Wichita, May 14, aged 57, of arteriolar nephrosclerosis with uremia

Barinbaum, Moses, New York City, Albertus-Universitat Medizinische Fakultat, Konigsberg, Prussia, Germany, 1911, died in the Lenox Hill Hospital May 25, aged 74, of carcinomatosis

Barry, Frederick Wheeler Ⓜ Coffeen, Ill, Washington University School of Medicine, St Louis, 1902, president of the Coffeen National Bank, on the staff of the Hillsboro (Ill) Hospital, where he died May 7, aged 83, of coronary thrombosis

Beals, Hugh Ⓜ St Paul, the Hahnemann Medical College and Hospital, Chicago, 1908, affiliated with Midway and Bethesda hospitals, died in La Jolla, Calif, May 2, aged 76, of cerebral thrombosis

Beck, Gerald Henderson, Glendale, Calif, University of Nebraska College of Medicine, Omaha, 1921, member of the American Academy of General Practice, died in the Glendale Sanitarium and Hospital April 4, aged 65, of cerebral hemorrhage

Brines, Osborne Allen Ⓜ Detroit, born in Algonac, Mich, April 19, 1893, Detroit College of Medicine and Surgery, 1927, specialist certified by the American Board of Pathology, fellow of the American College of Physicians, founding fellow of the College of American Pathologists, member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists, of which he was past-president, vice-president from 1951 to 1957, when he was the first American to be elected president of the International Society of Clinical Pathology, professor and chairman of the department of pathology at Wayne State University College of Medicine, received the Wayne University Alumni Award for distinguished service, veteran of World War II, consulting pathologist at the Veterans Administration Hospital in Dearborn, the Detroit Memorial Hospital, Woman's Hospital, and Sinai Hospital, pathologist and director of laboratories of the City of Detroit Receiving Hospital, died May 17, aged 67, of coronary occlusion

Brown, Roger Williams Ⓜ Ogden, Utah, Washington University School of Medicine, St Louis, 1945, member of the American Academy of General Practice, formerly an officer in the medical corps of the U S Naval Reserve, associated with the Thomas D Dee Memorial and St Benedict's hospitals, died May 11, aged 40

Burton, Samuel Hendren, Weston, W Va, University of Virginia School of Medicine, Charlottesville, 1897, past-president of the Central West Virginia Medical Society, veteran of World War I, died May 27, aged 87, of arteriosclerotic cardiovascular disease

Buyer, Edith S Michael Ⓜ New Rochelle, N Y, born in New York City Feb 1, 1894, Johns Hopkins University School of Medicine, Baltimore, 1918, member of the American Psychiatric Association, for many years medical supervisor for the board of education in New Rochelle, at one time an assistant in psychiatry at Columbia University College of Physicians and Surgeons in New York City, served on the staffs of the Vanderbilt Clinic of Columbia-Presbyterian Medical Center in New York City and the New Rochelle Hospital, during World War II was a Navy medical officer at the Waves Training School in the Bronx, died in Suffern June 5, aged 66, of cancer of the stomach

Callahan, William Michael, Rochester, N Y, University of Buffalo School of Medicine, 1921, veteran of World War I, on the staff of St Mary's Hospital, died May 22, aged 66, of coronary arteriosclerosis

Carls, Frederick George Ⓜ Riverside, Calif, University of Illinois College of Medicine, Chicago, 1914, died in the Riverside Community Hospital June 7, aged 74, of aneurysm

Carpenter, Harry Barron Ⓜ Portsmouth, N H, Bellevue Hospital Medical College, New York City, 1895, past-president of the Coos County Medical Society, veteran of World War I, served

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Ⓜ Indicates Member of the American Medical Association

as a medical examiner during World War II and for more than 20 years served as the local physical examiner for the Civil Aeronautics Administration, died May 25, aged 88, of cerebral hemorrhage

Case, James Thomas Ⓜ Santa Barbara, Calif, born in San Antonio, Texas, Jan 5, 1882, American Medical Missionary College, Battle Creek, Mich, and Chicago, 1905, professor and head of the department of radiology at Northwestern University Medical School from 1913 to 1947, when he became professor emeritus, in 1949 honorary professor of radiology at the University of San Marcos, Lima, Peru, specialist certified by the American Board of Radiology, past-president of the American Roentgen Ray Society, American Radium Society, and the American College of Radiology, which in 1955 presented him with its Gold Medal Award, last February was awarded the 1960 Gold Medal of the Centre Antoine Beclere of Paris, formerly member of the executive committee and president of the Chicago Tumor Institute, fellow of the American College of Surgeons and formerly member of its board of governors, fellow of the International College of Surgeons and formerly treasurer, honorary memberships included the medical, surgical, and radiological societies of Paris, London, Puerto Rico, Brazil, Scandinavia, Peru, Cuba, Mexico, Argentina, and Colombia, an honorary consul in the Dominican Republic, in 1924 was a delegate of the U S Army to the third Pan-American Scientific Congress in Lima, Peru, and in 1946 was a member of the American delegation to the Inter-American Congress on Radiology in Havana, for his service during World War I received a commendation and the Purple Heart, colonel in the medical reserve corps from 1920 to 1932, from 1932 to 1937 executive officer of the 108th medical regiment, 33rd division of the Illinois National Guard, decorated with Order of Merito Militar (Mexico) 1948, Cuban Order of Merit, Carlos Finlay, 1955, and Colombian Orden de Boyaca, 1955, editor of "Roentgen-diagnostics" published in four volumes, and of chapters in various medical books, for many years editor of *Annals of Roentgenology*, formerly editor of the *American Journal of Roentgenology*, at one time associate editor of the *American Journal of Surgery*, for many years associated with the Battle Creek (Mich) Sanitarium, where he was president of the board of trustees from 1944 to 1951, served on the staffs of St Luke's Hospital, Highland Park (Ill) Hospital, and Passavant Memorial Hospital in Chicago, director of the Memorial Cancer Foundation, associated with the Santa Barbara General Hospital and the Santa Barbara Cottage Hospital, where he died May 24, aged 78, of metastatic carcinoma of the lung, liver, and brain

Coke, Rogers Jr Ⓜ Aztec, N M, University of Texas School of Medicine, Galveston, 1953, interned at the Jefferson Davis Hospital in Houston, Texas, member of the American Academy of General Practice, on the staff of the San Juan Hospital in Farmington, died May 10, aged 44, of suffocation due to massive cellulitis of the neck

Cunha, Felix, San Francisco, born in Somerville, Mass, March 10, 1896, Tufts College Medical School, Boston, 1917, served as clinical instructor in medicine at the University of California School of Medicine, where he was lecturer in medical history and bibliography, fellow of the International College of Surgeons, member of the American Gastro-Enterological Association and the American College of Gastroenterology, of which he was president in 1952-1953, veteran of World War I, on the staffs of the Doctors, St Mary's, and Notre Dame hospitals, died May 17, aged 64, of diabetes mellitus

Delicate, Henry Brinkmann, Edwardsville, Ill, Washington University School of Medicine, St Louis, 1924, on the staff of St Elizabeth Hospital in Granite City, died in St Joseph Hospital, Highland, May 17, aged 61, of cerebral hemorrhage

Elmer, Walter Gray Ⓜ Philadelphia, University of Pennsylvania Department of Medicine, Philadelphia, 1897, member of the American Academy of Orthopaedic Surgeons, fellow of the American College of Surgeons, emeritus professor of orthopedic surgery at the University of Pennsylvania Graduate School of Medicine and at Woman's Medical College of Pennsylvania, veteran of World War I, died in the Abington (Pa) Memorial Hospital May 17, aged 87

Enstam, Carl John Harold, Los Angeles, the Hahnemann Medical College and Hospital, Chicago, 1920, veteran of World War I, died May 5, aged 68, of nephrosis

Forrest, George B, West Plains, Mo (licensed in Missouri in 1925), died May 5, aged 89, of coronary arteriosclerosis and carcinoma of the prostate

Harber, Abraham Roscoe, New York City, Cornell University Medical College, New York City, 1920, died in the Lebanon Hospital May 23, aged 64, of carcinoma of the liver

Warshaw, David Ⓜ New York City, Cornell University Medical College, New York, 1921, fellow of the American College of Surgeons, veteran of World War I, associated with Doctors Hospital, died in the Methodist Hospital, Houston, Texas, May 26, aged 65, of cerebral vascular accident

Williams, James Thomas, Wilkes-Barre, Pa, Jefferson Medical College of Philadelphia, 1931, veteran of World War II and received five battle stars and the Bronze Star for meritorious service, on the staff of the General Hospital, died May 26, aged 53, of coronary thrombosis

FOREIGN LETTERS

BRAZIL

Superillumination for Icterus Neonatorum—H C Ferreira and co-workers presented to the Associação Paulista de Medicina a report on an improved method of superillumination for the treatment of hyperbilirubinemia in neonates In certain conditions, high blood levels of bilirubin can damage the nervous system by provoking kernicterus The best currently used treatment of hyperbilirubinemia is replacement transfusion which, unfortunately, is associated with a high case fatality rate In the efforts to find a simpler solution for the problem, the authors tried the method proposed in 1958 by Cremer, who, using a beam of light of the zone 420 to 450 millimicron of the spectrum to transform bilirubin into biliverdin, treated nine neonates with good results

The authors constructed an apparatus with eight fluorescent lamps of 40 watts each, in a cylindrical reflector Completely naked except for a piece of gauze over the eyes, the patient is placed at a distance of 30 to 50 cm from the apparatus for periods of six hours alternated with two hours in complete darkness The authors series comprised 19 neonates The bilirubin level was always determined before and after and in some cases two or three times during the treatment The lowest bilirubin level was 19 2 and the highest was 32 6 mg per 100 ml The average weight of the patients was 3,315 Gm (about 7 lb), the range was 2,600 to 4,320 Gm

Of the 19 patients, one showed an anemia with spherocytosis, possibly in consequence of an anti-A antibody This patient required a replacement transfusion The bilirubin level in all cases was much lower after treatment, and lower than after blood replacement The average bilirubin level was 24 4 before and 17 9 mg after treatment The infant showing the best result had a fall of 11 6 mg of bilirubin per 100 ml in 24 hours and none had an increase of the bilirubin level, although this frequently occurs in untreated patients The authors concluded that the superillumination treatment is effective, simple, and without undesirable side-effects Although they believed it to be the treatment of choice, they found that replacement transfusion was necessary in some patients especially those with hemolysis

Geriatric Surgery—An increasing number of operations are being performed on elderly patients Operative risks in such patients have been reduced by better methods of anesthesia, control of water and electrolytes, blood replacement, and the use of antibiotics Paulino and Leite (*Hospital* 57 641, 1960) reported a series of 39 major operations on patients who were between 80 and 95 years of age There were only two operative deaths, 21 of the operations were for cancer It was possible to remove a malignant tumor from 10 patients, one of them, who had a gastric cancer, was still alive 6½ years after the operation

One 86-year-old patient survived one year after a pulmonary lobectomy, and died without evidence of malignant relapse The gallstones in older patients are almost always stones in the ductus choledochus which makes operation imperative If the basic principles for surgery in older persons is followed, the biliary operation can be performed with great safety An 84-year-old woman with jaundice, whose general condition was poor, was enjoying a normal and active life eight years after the operation In the preoperative care of older patients, the first diagnosis must include an evaluation of the patient's general condition Older patients require special psychological care They must be treated with great kindness, and their demands, often originating from habits of domination or dependency, must be satisfied Their old customs cannot be suddenly modified without unfavorable repercussion on their mind and, many times, with unpredictable psychic reaction

Arteriosclerosis, arterial hypertension, and pulmonary emphysema are frequent, sometimes associated with chronic bronchitis, bronchiectasis, or myocardial damage Healed myocardial infarction and bundle-branch block are frequent in patients over 70 but are without significant influence on operability Blood circulation depends largely on a good respiratory function, for the evaluation of which it is necessary to measure the pulmonary ventilation, the pH, oxygen saturation, and the total carbon dioxide content of blood Patients with bronchopulmonary disorders need preoperative respiratory gymnastics, postural drainage, and bronchodilatory and antibiotic medication

Symptoms of coronary insufficiency with anginal pains and retrosternal oppression during effort need special care and should be operated on only when it is impossible to defer surgery The evaluation of the renal function as well as the study of volemia are also fundamental to permit the indication of the necessary corrective measures Blood replacement during operation is important, but even more important is avoidance of blood loss by careful hemostasis Postoperative care in geriatric surgery must include observation of the pulse rate, blood

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The items in these letters are contributed by regular correspondents in the various foreign countries

pressure, early ambulation, adequate nutrition, and the prevention of urinary retention and fecal impaction

FRANCE

Azoospermia—H Bayle of Paris (*Presse méd*, April 23, 1960) performed exploratory operations on 350 patients with azoospermia In 70, the epididymodeferential anastomosis could not be made because of stenosis of the two deferent canals which was due, in most of the patients, to blennorrhagia, tuberculosis, or a common infection Of the 248 patients subjected to either bilateral or unilateral epididymodeferential anastomosis, the author reported the results obtained in 183, the other patients were lost for follow-up Of these 183 patients the azoospermia was cured in 138 (75%), and 61 couples subsequently had 95 children An improved operative technique now restores the passage of sperms in about 90% of the patients

The results of operation depend on the quality of spermatogenesis before and after the operation, the permeability of the excretory passages below the anastomosis, and the operative technique used Spermatogenesis is not arrested in case of obstruction of the excretory canal of the gland The process of spermatogenesis is maintained and preserved by the presence of large cells or spermatophages which phagocytize the retained spermatozoids accumulated in the epididymal tube which is distended above the obstruction These spermatozoids which cannot be evacuated during ejaculation are destroyed as foreign bodies Spermatogenesis is sometimes more active than spermatophagia This may cause rupture of the distended epididymal tube

After operation, the revival of spermatogenesis was delayed for several months and in some patients for two years Age of the patient and duration of the obstruction were the most important factors in the restoration of spermatogenesis Among the patients ranging in age from 20 to 25, 83% were cured, whereas among those aged 40 or more only 44% were cured In patients in whom the duration of the obstructions was five years, 70% were cured, and in those with obstructions lasting 25 years or more, 60% were cured A failure of the first operation does not preclude a second operation The author operated twice on 12 patients and good results were obtained in 7 of these In case of an operative failure, the libido was not affected

Prethcamide, a Respiratory Analeptic—Bouyard and Gum (*Thérapie*, no 6, 1959) gave prethcamide to 10 patients who had a diffuse respiratory insufficiency of bronchial, pleural, and parietal origin This drug, given orally in doses ranging from 150 to 200 mg, brought about subjective and spirographic improvement There was an effective increase in minute ventilation The drug was capable of greatly increasing the respiratory amplitude It acted as an analeptic on the respiratory centers No side-effects were noted Prethcamide may be used in anesthesiology and in patients in whom resection of a pulmonary segment causes failure in the respiratory center

Nylon Plaques in Inguinal Hernia—At the meeting of the Academy of Surgery in November, J Zagdoun and A Sordinas described the use of nylon plaques for the repair of inguinal hernia and eventration in 148 patients Instead of restoring the posterior wall of the inguinal canal, it was covered with a nylon plaque shaped in the form of a leaf and provided with a slot for the passage of the suture by sewing the edges of the plaque to the crural arcade and to the conjoined tendons In order to avoid the formation of serous effusions, as a reaction to the operation, a sandbag was placed on the inguinal region In order to prevent rejection of the plaques due to sepsis, the skin should be in excellent condition, and there should be no foci of infection in the adjacent area Of the 148 patients operated on, relapses occurred in 8, 7 of which were located at the opening of the inguinal canal The authors believed that nylon plaques should always be used when the nature of the hernia, the condition of the walls, or the age of the patient threatens a recurrence

GERMANY

Anthrax—W Mohr of Hamburg (*Landarzt*, 36:9, no 1, 1960) stated that anthrax is rarely seen in Germany It occurs almost exclusively in persons who work with skins and furs In Germany from 1949 to 1958, 77 cases of anthrax of the skin or anthrax edema were observed

Anthrax serum is no longer used Penicillin in doses of 400,000 to 1,000,000 units or 1 to 2 Gm of tetracycline or oxytetracycline is given immediately, in order not to lose precious time, after obtaining material for culture and direct examination As soon as the sensitivity tests are concluded, treatment is continued with only that antibiotic which proved most effective The severe cases of anthrax septicemia require general treatment, especially of heart and circulation, in addition to the specific medication In patients with an especially great tendency to edema, administration of hydrocortisone or a related preparation has proved beneficial Surgery is contraindicated In the author's series of 33 patients, there were no deaths, but in two cure was incomplete and an occupational pension had to be granted In the total series of 77, there were 8 deaths including 1 in a patient with anthrax of the lung and 1 with anthrax meningitis Of the 69 who survived in all of Germany, 8 were granted a pension because of incomplete cure Sequelae of anthrax septicemia were myocardial damage, circulatory dysfunction, and persisting neurovegetative disturbances It is important that treatment is instituted early in order to achieve complete cure

Differential diagnosis from staphylococcic carbuncle is often difficult Little pain, accompanying edema, absence of lymphangitis, and initial mildness of pain in the regional lymph nodes are suggestive of anthrax carbuncle Necrotic herpes zoster may also resemble anthrax, but generally it can be said that the anthrax carbuncle has a pathognomonic form characterized by a central, blue-black, firm area of tissue necrosis, an elevated ulcer margin (sometimes with vesicle formation), and extensive edema The diagnosis can be definitely established only by microscopic and cultural demonstration of the anthrax bacillus

Infant Mortality—H Muller (*Deutsche med Wchnschr* 84 2331, 1959) reported that, in Germany and Austria, statistics showed an increase in infant mortality in the third month of life, especially in girls This is in contrast to observations in other countries where infant mortality continually decreases from the first month onward Since this trend was not found in German statistics for previous years, the cause was sought It was first thought that this increase might be related to the maternity protection law which provides that mothers may resume work six to eight weeks after parturition The relative mortality among illegitimate children was also traced The death rate was higher for boys than for girls The mortality among illegitimate children was about twice that of legitimate children in all months and years of life

The causes of death were studied, but unfortunately the determination of the cause of death in infants is often difficult even in cases in which autopsy is performed The statistics nevertheless showed that deaths in the second month were mostly due to nutritional disorders and in the third month to respiratory diseases If the increase in deaths in the third month were related to the maternity protection law, a predominance of nutritional disorders was to be expected, since breastfeeding is usually stopped at the time of return to work A cause that may come into consideration is, therefore, interstitial plasma-cellular pneumonia This has an incubation time of 40 days, and this is why most children do not become ill with it before the end of the second month Incipient pneumonia becomes severe only after several days and, in most cases, is fatal The disease was rarely observed after the fifth month of life It is more or less endemic in most pediatric hospitals

Since nursery homes always have many children from unmarried women, illegitimate infants are more exposed to infection than legitimate children More girls than boys (100 93) die of interstitial pneumonia, in contrast to other diseases Since efforts have been made in recent years to prevent the epidemic spread of interstitial pneumonia in pediatric hospitals, the peak of infant mortality in the third month of life has decreased, and since interstitial pneumonia is practically unknown in Scandinavian countries, the United Kingdom, and the United States, the increase in infant mortality in the third month was not observed in these countries

Triiodothyronine and Arteriosclerosis—Pezold and Droege, of Berlin (*Arzneimittel-Forsch* vol 9, no 561, 1959) stated that after the individual constant of the lipid level under the set of test conditions had been determined in preliminary tests, 10 healthy subjects were given 60 mcg of triiodothyronine by mouth daily for seven days Lipid levels declined in all, serum cholesterol levels in nine, and phospholipid levels in five A series of 38 patients with clinically manifest arteriosclerosis were given 60 mcg of triiodothyronine daily for one week (group 1), 30 to 90 mcg for two weeks (group 2), or triiodothyronine for two weeks, followed by a placebo for the same period, and again by triiodothyronine (group 3) In group 1, there was marked reduction in total lipid levels in 9 of 10 patients In group 2, there was a decrease, in some cases marked, of total lipid level in 8 of 14 patients in 4, the value increased, and in 2, it remained unchanged In group 3, the lipid levels decreased during triiodothyronine treatment, and increased during administration of the placebo Triiodothyronine, therefore, effected in this short-term trial a decrease in the serum lipids of both healthy and arteriosclerotic subjects The dose for arteriosclerotic patients should not exceed 20 mcg a day, otherwise side-effects may occur

INDIA

Adrenal Function in Infectious Hepatitis—P N Wahi and co-workers (*Indian J M Sc* 14 302 [April] 1960) investigated adrenal cortical function in 46 patients with infectious hepatitis by carrying out a battery of eight adrenal cortical function tests The adrenal function tests used were urinary uric acid response to ACTH, serum cholesterol response to ACTH, urinary 17-hydroxycorticosteroid response to ACTH, eosinophil response to ACTH, determination of urinary 17-hydroxycorticosteroid, urinary uropepsin, and urinary 17-ketosteroid levels, and estimation of the serum sodium level The urinary uric acid response to ACTH was subnormal in 22 patients, the serum cholesterol response was deficient in 24, the urinary 17-hydroxycorticosteroid response was below normal in 24, and eosinophil response was subnormal in 17

The responses of urinary uric acid and 17-hydroxycorticosteroids and serum cholesterol ran parallel to each other but had no correlation with the eosinophil response The excretion of urinary 17-hydroxycorticosteroids was subnormal in 11 patients, the urinary uropepsin level was diminished in 13, the excretion of urinary 17-ketosteroids was deficient in 37, and the serum sodium level was reduced in 16 The mechanism involved in the production of impaired adrenal cortical function in patients with infectious hepatitis was not determined, but the authors believed that both the stress of infection and hepatic functional damage could be responsible Since the responses to adrenal function tests used in this study depended partly or wholly on glucocorticoid hormones, the results would seem to indicate a state of hypoglucocorticoidism in this disease

Cellular Reactions After Tumor Growth—B D Baruah (*Indian J M Sc* 14 308 [April] 1960) transplanted Rd/3 rat tumor and Walker carcinoma in albino rats and killed the animals after 17 to 30 days In another series, tumors were induced with dibenzanthracene For tumor inhibition and regression, a small dose of this same substance was injected intraperitoneally During the progressive stage of the tumor, the lymph nodes and spleen showed a marked increase in weight after both tumor transplantation and induction The changes, however, were more marked with the transplanted than with the induced tumors The increase in weight was unrelated to the incidence of metastases The weight of the adrenals was increased and that of the thymus decreased

Microscopically the lymph nodes and spleen showed an increase in plasma cells accompanied by diminution of lymphoid tissue The plasma cells became much more numerous as the tumor grew, and a significant correlation was noticed between the tumor weight and plasma cell response in these organs Lymph nodes with secondary deposits showed a markedly diminished plasma cell reaction The local reaction of the host around the tumor during growth was slight, and there was a scanty cellular infiltration consisting of lymphocytes, macrophages, plasma cells, and a few polymorphonuclear cells The lymphocytes predominated in this reaction, and plasma cells were few or absent The peripheral blood contained no plasma cells at any stage

During regression, the weight of lymph nodes and spleen showed diminution The plasma cell reaction in these organs also diminished and gradually returned to normal as the tumor cells disappeared Locally, there was increased host reaction during regression, consisting of increased accumulation of plasma cells without any appreciable alteration in lymphocytes When regression was complete and tumor cells were no longer seen histologically, the local reaction was scanty and consisted of areas of fibrosis and a few plasma cells The peripheral blood again showed no plasma cells The animals became resistant to a second graft of the same tumor after regression of the first transplant

Heat-killed tumor grafts did not elicit local or distant plasma cell response and failed to produce immunity against a subsequent inoculation with a living tumor graft The authors concluded that the plasma cell response as seen in this study constitutes the morphological manifestation of an immune reaction due to antigenic stimulation by these tumors and is related to the formation of antibodies The immunity thus produced conforms to the immune state generated by bacteria and foreign proteins There was no evidence in this study to suggest the lymphocytic origin of plasma cells, but there was reticulum cell hyperplasia in the lymph node and spleen All gradations from reticulum cells to mature plasma cells were observed, thus suggesting that the reticulum cells contribute to the formation of plasma cells

NORWAY

Operation for Weak Ankle—Henrik Storen reported (*Acta chir scandinav* 117 501-509, 1959) use of a new operation on six patients (on one of whom it was done bilaterally) to treat insufficiency of the lateral ligaments of the ankle The operation included two important features (1) transposition of a living tendon and (2) no interference with the specific peroneus brevis function It thus had the advantages but not the disadvantages of a tenodesis in which the peroneus brevis tendon is transposed and, the specific function of the muscle is thereby eliminated This, in the author's opinion, might upset the natural muscular balance of the foot A drawback of the method was the fact that it had to be performed in two stages, but between operations the patient was fully able to work

In the first stage the median third of the tendo achillis is dissected free from its muscular attachment and its insertion on the tuberosity of the calcaneus is retained The free dissected end is pulled anteriorly past the tendo achillis, guided subcutaneously to the lateral malleolus, through this in a drill tunnel, through another drill tunnel in the neck of the astragulus to the sinus tarsi, and finally it is anchored to the bifurcated ligaments or intraosseally in the calcaneus, with use of a pull out wire through the sole The second stage should not be performed less than four months, preferably longer, after the first operation The posterior part of the transposed tendon is freed from the insertion on the tuberosity of the calcaneum and is fixed intraosseally through a pull out wire in the calcaneum at the insertion of the ligamentum calcaneofibulare, thus following the course of this ligament So far the method has given satisfactory results in all patients, though the ankles operated on have been subjected to great stress The observation time after operation ranged from one to eight and one-half years (average three)

Esophagitis After Total Gastrectomy —A follow-up study made five to nine years after total gastrectomy for cancer revealed esophagitis of a mild to moderate degree in eight of nine patients, according to Nils Helsingen Jr (*Acta chir scandinav* 118 190-201, 1959-1960) Esophagojejunal anastomosis, end to side, was the method of reconstruction An additional Braun's enteroanastomosis was performed on six patients, and in one of them the afferent jejunal limb was also occluded Esophagitis occurred in spite of these additional procedures The incidence of this complication as reported in the literature varies widely, which might be attributed, in part, to the use of different types of reconstruction On the other hand, the diagnostic criteria at times were obviously insufficient which might also explain some of the controversial opinions Further, the possibility of tumor recurrence must always be considered Endoscopic examination is necessary for a final evaluation of this complication

All but one of the patients in the present series with esophagitis complained of episodes of heartburn and regurgitation Mild hysphagia was present in four patients and ptyalism was a symptom in five On the whole, symptoms were less prominent than for the first year or two after operation No esophageal stricture was found, and dilatation of the esophagus had not been required in any of the patients Signs of megaloblastic anemia were found in three patients at the follow-up examination Regurgitation could be reduced through simple postural aids and dietary restrictions Prevention of esophagitis might possibly be achieved by certain operative modifications No general agreement has yet been reached on this point however A reflux of duodenal contents into the esophagus appeared to be an important etiological factor though other factors might also prove to be operative

UNITED KINGDOM

Radiologic Safety Program —According to the *British Medical Journal* (May 19, 1960) the committee appointed by the prime minister to investigate the accident to No 1 Pile at Windscale in October, 1957, had made its report This called attention to the urgent need for specialists trained in the principles and techniques of radiologic protection To make the best use of highly trained staff the committee recommended the establishment of a national radiologic advisory service, organized on a regional basis, which would provide both advice and technical assistance to departments and firms requiring it Such a service would be linked with the universities, regional hospital boards, local governments and the industry in the region It would incorporate the existing Radiological Protection Service set up several years ago by the Medical Research Council and the Ministry of Health and would carry on the activities of this organization within the larger framework

The committee recognized that the hospital service already possesses the necessary radiologists, physicists, and radiographers and that any necessary increase in numbers can be met by the present internal training schemes The conditions of service, however, may have to be made more attractive in order to maintain recruitment in face of increasing competition Other recommendations of interest to the medical profession are that radiologic health and safety should be taught to students taking the diploma in public health and that the basic medical curriculum might include enough instruction in the use and hazards of ionizing radiation to give a clear picture of the scientific principles involved and the significance of the effects

Electronic Fluoroscope —A new electronic fluoroscope which produces a picture of the patient on a television screen has been demonstrated at the King Edward VII Memorial Chest Hospital The new machine has the following advantages over conventional roentgenographic screening (1) doctors and patients are exposed to much less radiation, (2) examinations of, say, the heart can be made in daylight, thus eliminating the need for the radiologist to adapt his eyes to total darkness, (3) patient is reassured by being in light and not in darkness, (4) investigation is speedy, (5) picture is bright and clear, (6) cinecamera can be used to make a continuous record of the large fluoroscopic images, (7) picture can be magnified and also "held" for prolonged examination, and (8) it is possible to operate additional independent television monitors, and this is valuable for teaching for an examination can be shown to several hundred students gathered at a distance

Bruise Prevention —The Amateur Boxing Association was asked by its medical officer to sanction the general use of streptokinase-streptodornase by boxers before bouts Tests made over nine months convinced him of its value in preventing bruising and in promoting healing of cuts A total of 494 boxers cooperated in the investigation Of these, 247 took the drug before boxing, the other 247 took dummy tablets of identical taste and appearance The most significant result was a 50% reduction in general bruising among those who took the streptokinase-streptodornase Boxers who received cuts and were treated with the drug afterwards were fit to fight again in two weeks

CORRESPONDENCE

EFFECTS OF CYTOTOXIC AGENTS ON THE FETUS

To the Editor.—The paper by Sokal and Lessmann in THE JOURNAL, April 16, page 1765, on the effects of cancer chemotherapeutic agents on the human fetus is a valuable contribution, but I believe that the statement in their summary that "other drugs (than aminopterin) have proved far less toxic for the fetus than would have been anticipated from theoretical considerations or animal experiments" is misleading and potentially dangerous. The animal data indicate that antimetabolites are likely to cause abortion and resorption of embryos if administered early in gestation and fetal malformation if administered later during the major period of organogenesis (i. e., 10th to 12th day in the rat). These periods correspond roughly to the first trimester of human pregnancy, particularly to the first eight weeks. The second third of the 22-day rat pregnancy is not comparable to the second trimester of human pregnancy.

Only three patients given 6-mercaptopurine in the first trimester of pregnancy are recorded in Sokal and Lessmann's table. Two of these pregnancies resulted in premature normal-appearing but nonviable infants, and the third resulted in a premature infant with multiple congenital anomalies, who died after two months. Since treatment of pregnant animals with cytotoxic agents later in gestation (i. e., after the 13th day in rats) does not usually result in fetal malformation, it is not surprising that 6-mercaptopurine, nitrogen mustard, and other agents administered to human beings in the second and third trimesters have not resulted in significant abnormality. The authors point out that folic acid antagonists can induce both abortions and fetal abnormalities when administered during the first trimester of pregnancy, but there is experimental and clinical evidence that 6-mercaptopurine and other antimetabolites may have similar properties if given in adequate doses prior to completion of organogenesis in the mammal.

Until further data are available, it seems most important to emphasize that any cytotoxic agent administered during pregnancy, especially during the first trimester, is a potential hazard to the developing fetus. If abnormalities are not manifest at birth, they may appear in subsequent years. When or whether one used such agents during pregnancy depends on one's aim in therapy in the particular case concerned. Detailed discussions of this problem have appeared previously (Smith, Sheehy, and Rothberg: A. M. A. Arch. Int. Med. 102:777 [Nov.] 1958; Rothberg, Conrad, and Cowley: Am. J. M. Sc. 237:194 [Feb.] 1959).

On the basis of the available evidence, it would appear that the cancer chemotherapeutic agents should be used with particular caution during pregnancy, if at all, and it is the physician's responsibility to know as accurately as possible the existence and stage of pregnancy in his patients. A similar precaution might be appropriate for many other drugs commonly used in clinical medicine.

I should like to echo Sokal and Lessmann's appeal for detailed long-term follow-up of infants born to mothers treated with cancer chemotherapeutic agents. I hope these authors will be able to provide subsequent reviews of this problem in future years.

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SUPERFICIAL FEMORAL VEIN LIGATION

To the Editor.—We appreciate the abstracting of our article, "Results Obtained by Superficial Femoral Vein Ligation," (Keisker and Bowers: Surgery 47:224 [Feb.] 1960) in THE JOURNAL, May 14, page 208. In the abstract, however, there is a mistake concerning the statistical analysis of the follow-up studies which would tend to influence the reader against superficial femoral vein ligation. In the original article appears the following statement: "Thirty-eight patients revealed no swelling by observation, history, or measurement. The swelling was mild in 38 cases and severe in 10 cases." The abstract, however, states, "Thirty-eight patients complained of severe swelling of the legs, and 10 complained of mild swelling." We sincerely believe in the efficacies of the operation for the reasons mentioned in the article and hope that the impression given by the abstract can be corrected.

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CONGENITAL LESIONS OF THE HIP

To the Editor.—I would like to comment on the article by Harris, Lipscomb, and Hodgson on the diagnosis of congenital lesions of the hip, which was published in THE JOURNAL, May 21, page 229. I note that 11,010 infants were examined on the first day of life and again on the fifth day, and 90% of them were examined at regular intervals for six years. If the roentgenograms shown in the article are characteristic, none of the patients had shielding of the gonads, and one would wonder as to the quantity of the gonadal dose of radiation as a result of these studies. It would seem from the experience reported in the radiologic literature that the criteria which are available for the roentgenographic diagnosis of congenital hip disease are widely known and understood, and I can see little need to subject 11,010 infants to repeated examinations and increase the unnecessary gonadal dose from the medical use of x-rays. I appreciate the fact that the radiology department at the Mayo Clinic is an outstanding one, but I also must conclude that, at times, one's zeal overcomes judgment. This seems to be the situation in this study.

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DRUG SAMPLES FOR CHARITY HOSPITAL

To the Editor.—I have read Sonneland's letter to the editor in The Journal, May 21, page 295, and I would like to request Dr. Sonneland and any other physicians who throw their samples in the wastebasket to send these samples to me at the above address. I am collecting samples of drugs for the Albert Schweitzer Hospital in Haiti. This is a charity hospital in the Artebonite Valley. Any physicians wishing to send samples directly to the hospital may use this address:

Albert Schweitzer Hospital
c/o Allan & Baussan
P. O. Box 1304
Port-au-Prince, Haiti

If they would like further information regarding the Albert Schweitzer Hospital, they may obtain it from the Grant Foundation, 525 William Penn Pl., Pittsburgh 19.

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USE OF THE WORD "ADENOCARCINOMA"

To the Editor.—The excellent article by Linden and co-workers entitled "Validity of Pathological Diagnosis of Breast Cancer," in The Journal, May 14, page 143, is reassuring to the practicing pathologist. The fact that 95.6% of the diagnoses of breast cancer were confirmed by three independent experts on material arising from a large number of institutions is a tribute to the uniformly high level of practice of anatomic pathology in the United States and to the American Board of Pathology.

Less pleasing to the practicing pathologist is the tabulation showing an incidence in these breast cancers of 41.2% "adenocarcinoma" and 10.3% "ductal carcinoma." It is difficult to believe that eminent pathologists believe that duct carcinoma constitutes only 10% of breast cancers. In fact, the article tries to gloss over the unfortunate classification by referring to comparisons between the histological and histogenetic considerations. Although, in the words of Fred Waldorf Stewart, "Classification of tumor types is one of the bugbears of pathology," it is still a fact that we should make some effort to agree on a reasonable terminology. For example, Ackerman, in his classic textbook, states that 5% of breast cancers are of lobular carcinoma type (he does not use the word "adenocarcinoma" at all) whereas the other 95% are of duct epithelial origin, using approximate percentages throughout. As William Boyd points out, "many subgroups can be recognized in the field of breast cancer, depending on whether the pathologist is a splitter or a lumper," but there is a big difference between lumping only 10% of the cases together as duct cell carcinoma and putting 95% under the same heading.

The use of the word "adenocarcinoma" in breast cancer is justifiable only if we wish to regard the entire breast as an overgrown sebaceous gland. The word could be best relegated to those few specific instances of true lobular or acinar carcinoma.

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A PLEA FOR THE UNCONCEIVED

To the Editor.—I would like to protest an otherwise fine and pertinent editorial, "A Plea for the Unconceived," in The Journal April 16, page 1774. I believe I capture the mood of the editorial when the author states: "Ironically, one group of scientists assures us of mass genetic death by radiation, another group are as insistent that we are so fertile that the planet will have standing room only." But I must part company with him when he goes on to say: "Obviously, both cannot be correct." I am reminded of the issue of the *New Yorker* (Jan. 19, 1946) which was devoted to the Smyth Report. Most of it was pretty grim, but it had the *New Yorker* touch. In a box on the front page of the article appeared the following poem: "Man split the atom/ Blew him all to hell/ God rolled over in his sleep/ and muttered All is Well." If it were to be a nice clean job, it would be obvious that both possibilities mentioned could not be correct. The real problem is that the genetic death will be not massive but scattered and cumulative, and there would be a growing burden of congenital defects. In other words, both groups of scientists can be correct.

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QUESTIONS AND ANSWERS

RECEDING GUMS

To the Editor —*What are the causes and treatment for receding gums when there is no evidence of infection and the teeth are excellent?*

R S Singley, M D, Altus, Okla

Answer —The most common cause of recession of otherwise healthy gums is aggressive, improperly directed toothbrushing The gingiva is worn away, and the root surfaces are exposed Alignment of the teeth in the arch affects susceptibility of the gums to recession under such circumstances Teeth which are malposed so that they bear the brunt of the brushing action present the greatest recession Some observers believe that improper relationship of the mandibular teeth to the maxillary teeth in chewing leads to trauma, which is an additional causative factor of recession of otherwise healthy gums

The treatment of such recession consists of improvement in toothbrushing technique and, if possible, correction of the position of the teeth Adjustment of the functional relationships of the teeth by judicious grinding may also be included as a precautionary measure Recession may be stopped, but complete restoration of the gums is unlikely The most important cause of gingival recession is inflammation Sometimes the gums appear outwardly healthy but there is inflammation of the inner aspect of the sulcus Careful check for local irritants and their elimination are worthwhile precautionary measures in all patients with recession, despite the fact that the gums outwardly appear healthy

NUCLEUS PULPOSUS

To the Editor —*A patient had an injury to an intervertebral disk in 1952, and in 1955 a plastic disk was inserted The operation was apparently unsuccessful, since the man has more back pain now than he had before I believe that he would be helped if the plastic disk were removed and a fixation operation done Am I right?*

Robert E Terry, M D, Cuba City, Wis

Answer —It is true that plastic intervertebral disks are being used, in spite of the fact that it appears illogical to replace a movable disk with one made of a firm plastic material Difficulties arising from the use of such disks have been reported Unfortunately, once a plastic intervertebral disk has been emplaced, it is difficult to remove it If, however, the plastic disk in question could be removed, and if the spinal column could be fused in the affected area, relief of the pain might be obtained Sometimes, if the plastic material cannot be removed, performance of fusion alone will bring about relief All such patients referred to this consultant were referred because of failure of such disks and complications arising from their presence

CORONARY OCCLUSION

To the Editor —*A 42-year-old man had a coronary occlusion in April, 1958 In July, 1959, he was started on continuous bishydroxycoumarin therapy He also takes pentaerythritol tetranitrate His condition seems to have improved somewhat on the anticoagulant therapy 1 Is continuous anticoagulant therapy justified in this patient? 2 Instead of therapy with bishydroxycoumarin alone, would there be any benefit from substitution of 200 mg of heparin given subcutaneously daily? 3 If the patient could not afford this much heparin daily, would it be helpful to continue to give him bishydroxycoumarin and in addition 50 to 75 mg of heparin subcutaneously every other day? 4 Is there any rule that can be used to determine whether a patient may benefit by the addition of heparin to his treatment rather than from use of a coumarin derivative alone? 5 Has anyone proposed that heparin may be beneficial in those persons whose plasma becomes clear of lipids slowly after meals but not any more helpful than a coumarin derivative given orally, if the lipids cleared from the plasma at a normal rate after a meal? 6 Might this patient benefit by having his serum neutral fat level determined or a fat tolerance test made to determine whether lipids clear from his plasma at a normal rate? 7 Under what circumstances should a patient be placed on a diet which is free of lipids at various intervals?*

Joe M MacCurdy, M D, Baton Rouge, La

Answer —1 Continuous anticoagulant therapy is optional It may be justified in this patient if the facilities are easily available to him and he wishes to continue on the therapy 2 No demonstratable benefit can be predicted by the substitution of 200 mg of heparin given subcutaneously daily for bishydroxycoumarin It would greatly increase the cost of anticoagulant therapy, and, over a time, the subcutaneous tissue would become scarred and badly discolored from hematomas as a result of the constant injection of heparin 3 There would be no advantage in injections of heparin unless the patient became more acutely ill or developed a marked increase in the number of anginal at

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The answers here published have been prepared by competent authorities They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply Anonymous communications cannot be answered Every letter must contain the writer's name and address, but these will be omitted on request tacks 4 The only significant means of determining whether heparin should be tried instead of coumarin derivatives would be failure to control the anginal or thromboembolic complications while the patient is given bishydroxycoumarin alone

5, 6, and 7 The question of the relation of the postprandial lipemia to myocardial infarction or the progression of atherosclerosis is still in an experimental phase Any answers to these questions would be largely hypothetical Evidence does suggest that if a patient is obese or has a high serum cholesterol level it may be beneficial for him to be placed on a diet low in saturated fats and cholesterol If he is thin but has a high cholesterol level it would be theoretically desirable to place him on a diet low in saturated fats, with free substitution of unsaturated fats

RETURN OF UROBILINOGEN AFTER RELIEF OF OBSTRUCTION

To the Editor —*Have there been any studies on the time of appearance of urobilinogen in the urine after the alleviation of complete obstruction of the common bile duct?*

M D , Illinois

Answer —Urobilinogen usually appears in the urine within 24 hours after a complete biliary obstruction or a complete cessation of bile flow from any cause has been relieved, so that bile has regained access to the intestine This is of particular value in recognizing beginning improvement in patients with severe hepatitis in whom there has been complete or almost complete cessation of bile flow on an intrahepatic basis It also helps to recognize intermittent obstruction, such as that due to calculus With carcinomatous biliary obstruction urobilinogen is much less likely to return to the urine once the complete obstruction has become established In some patients, however, especially those with carcinoma of the ampulla or polypoid common duct tumors, the obstruction is intermittent

Broad-spectrum antibiotics, such as the tetracyclines, neomycin, and erythromycin, characteristically interfere with urobilinogen formation in the intestine and cause disappearance of urobilinogen from the urine The urobilinogen may reappear in the urine in relatively reduced amounts after a variable period, even when the antibiotic treatment is continued

The presence of excessive urobilinogen in the urine is believed to be related to at least a transitory hepatic dysfunction It is most often encountered when there is definite hepatic injury or disease In the presence of discrete foci of disease, such as carcinomatous metastases, an increase of urobilinogen in the urine is much less likely to occur In the presence of renal insufficiency with azotemia, urobilinogen is seldom excreted in the urine in any excess and may not be demonstrable at all A high fever of any type is likely to be associated with excessive urobilinogen in the urine, probably due to mild hepatic injury

APHTHOUS STOMATITIS

To the Editor —*A 16-year-old boy has had recurrent aphthous stomatitis for several years He has been treated with vitamins, repeated smallpox vaccinations, local astringents, and other forms of local treatments without success There is no family history of this disorder He plays a trombone in the school band and this activity seems to aggravate the condition During the summer when he discontinued playing the trombone, the condition subsided almost completely He does not remember ever having the ulcers before playing the trombone Could this be a contact sensitivity from the metal in the trombone mouthpiece? Most of the ulcers are at an area which would be in contact with the mouthpiece, although occasionally ulcers appear elsewhere in the mouth Can any preventive measures be taken so that he can continue to play his instrument?*

H L Tindall, M D , Christiana, Pa

Answer —From the information supplied it would be unlikely that the condition described is caused by any specific contact sensitivity to the metal from the trombone mouthpiece Contact sensitivity reactions are generally not sharply outlined to the extent of causing circular or oval aphthous-type ulcers There would be a more obvious tendency to diffused reaction Physical trauma from repeated application of the mouthpiece to the lips could conceivably act as a trigger mechanism setting off the aphthous reaction It would not be of any help to perform patch tests with material from the mouthpiece There would not seem to be any way of altering the mouthpiece in any beneficial manner If not already tried, I would suggest the therapy recommended by Weekes (*New York J Med* 58 2672 [Aug 15] 1958) He dissolved two Lactobacillus suspension tablets in the mouth with milk, four times daily for several days This may be repeated as indicated, if helpful

CHORIORETINITIS

To the Editor —*What is the proper treatment for chorioretinitis, especially in patients with no other abnormalities? They seem to respond to vitamins and steroids, but in some relapses occur*

J Will Fleming Jr , M D , Moberly, Mo

Answer —The management of chorioretinitis requires extensive diagnostic studies, treatment of specific cause, if found, and nonspecific treatment Toxoplasmosis, histoplasmosis, tuberculosis, syphilis, and brucellosis are among the possible etiological factors Allergy to foods is a possible cause Such foods as cream, as pointed out by Leopold, may contain a causative organism A uveitis diagnostic kit may be obtained from the American Academy of Ophthalmology and Otolaryngology Treatment may require only antibiotics if a bacterial cause is discovered If response is inadequate, antibiotic therapy should be stopped Nonspecific therapy includes corticosteroids, salicylates, foreign protein, and empirical desensitization by vaccines If corticosteroids are used in a tuberculous patient, streptomycin and para-aminosalicylic acid (PAS) should also be used

It is not possible to give specific suggestions for the *treatment of chorioretinitis in general* Each patient must be treated individually Treatment may extend over weeks or years, depending on the nature of the disease, the type of therapy indicated, patient response, and complications, if any For a discussion of foreign protein therapy, see Gifford's "Ocular Therapeutics" revised by Vail (Philadelphia, Lea & Febiger, 1948) If a corticosteroid is given before a foreign protein, it should be continued throughout the period of foreign protein therapy For the general subject, see Woods' "Endogenous Uveitis' (Baltimore, Williams & Wilkins Company, 1956) An outline of "Modern Therapy of Uveitis," prepared by Dan M Gordon, M D, in connection with a scientific exhibit on this subject (presented at Pennsylvania-New Jersey Academies of Ophthalmology and Otolaryngology, Atlantic City meeting, 1960), may be obtained from Dr Gordon, Cornell University Medical College

DUODENAL ULCER

To THE EDITOR —*I understand that a pH of 4 to 5 is necessary for the healing of a duodenal ulcer Of the many antacids available, which one and what dose has the greatest neutralizing effect on the gastric contents?*

Sigmund R Nowak, M D, Baltimore, Md

ANSWER —There is no direct evidence in man that a pH of 4 to 5 of either gastric or duodenal contents is necessary for healing of a duodenal ulcer Peptic hydrolysis in vitro of certain substrates and inhibition of fibroblast growth in tissue culture are increased below pH 4 to 5 Duodenal ulcers heal without the use of antacids or apparent decrease in gastric acid production Ulcers are produced by irrigation of the small intestine in dogs with acid-pepsin mixtures more readily at pH 1 57 than 2 28 This pH change in gastric contents of man for 2 to 10 minutes follows ingestion of usual doses of aluminum hydroxide gels Limited studies of duodenal pH show little relation between gastric and duodenal pH changes after use of antacids Gastric emptying necessitates eight times more antacid in vivo than in vitro Calcium carbonate with the deterrents of alkalosis, renal lithiasis, and constipation least expensively produces a gastric pH of 4 for 16 hours daily at $48 a month, aluminum hydroxide liquid or tablets at $59 to $95 a month, aluminum amino acetate at $100 a month, and sodium carboxymethyl cellulose at a cost of about $1,000 a month Further study may show minor pH changes from feasible doses of antacids related to ulcer healing Meanwhile, clinicians generally agree most antacids relieve ulcer pain

ANSWER —Magnesium trisilicate (U S P) is considered by pharmacologists to be the most active neutralizer of gastric acidity, since 1 Gm neutralizes about 155 ml of 0 1 *N* hydrochloric acid It is a local acting antacid, and barring possible absorption of the magnesium ion in excessive amounts, should not cause distress in large doses, 4 Gm may be given, or more to a point where catharsis occurs

LABYRINTHINE HYDROPS

To THE EDITOR —*Are there any reports on the use of the steroids in patients with labyrinthine hydrops? If so, what preparations were used, in what dosage, and what were the results?*

Walter W Stebbins, M D, St Petersburg, Fla

ANSWER —This consultant knows of no reports on the use of steroids in the actual treatment of labyrinthine hydrops H B Perlman and co-workers have used steroids in clinical experiments in which they wanted to raise the sodium content of the body tissues in a group of patients suffering from this syndrome

It is believed that the use of the steroids is contraindicated in labyrinthine hydrops if the following facts are considered concerning the physiology of the labyrinth and the accepted etiology and pathology of the syndrome Dohlman, in a paper read before the New York Academy of Medicine, Section of Otolaryngology, at its meeting in April, 1959, showed that the fluid in the inner ear is a solution of polysaccharides, which has been shown by Catherine Smith to contain definite amounts of potassium and sodium, as well as protein substances

Dohlman's experiments indicated that the membranous labyrinth is an apparatus for producing a flow potential That is, when a polysaccharide solution enclosed in a narrow tube and containing sodium and potassium is made to move, it produces an electrical potential which is positive when the fluid moves in one direction and negative when it moves in the opposite direction H L Williams and Fowler and Fowler, in separate papers, have suggested that labyrinthine hydrops is prone to occur in patients who inherit a tendency to develop an imbalance in the autonomic nervous system When such patients are under tension or apprehension, there is a vasoconstriction at the arteriocapillary junction which, according to Knisley, favors blood sludge formation Distal to the point of vasoconstriction and due to an increased permeability of the vessel walls, there is a transudation of the liquid elements of the blood into the fluid of the labyrinth This causes a change in the chemistry and the quantity of the labyrinthine fluids resulting in a labyrinthine hydrops

Use of steroids is contraindicated in psychoneurotic patients Most of these drugs cause an increased retention of sodium and hence favor edema Although triamcinolone does not produce an increased concentration of sodium in the tissues, neither does it reduce the sodium that is already present Since, in the treatment of labyrinthine hydrops, an attempt is made to reduce the effects of tension and apprehension in the patients by psychotherapy, an attempt is also made to restore the labyrinthine fluid to a normal state insofar as its chemistry is concerned and to reduce edema of the labyrinth In view of these facts, this consultant believes that giving steroids is not a rational treatment of this syndrome

LACTOBACILLUS AND DENTAL CARIES

To the Editor —*A local dentist places great emphasis on the Lactobacillus count in children's mouths in his treatment of dental caries A 10-year-old girl who has had recurrent cankers for the past four months, which are helped only by penicillin and vitamin C therapy, was referred to the dentist because of many carious teeth He reported a Lactobacillus count of over 3,000,000 per cubic centimeter This is the highest count he has ever observed, and he wondered whether this could be due to prolonged therapy with penicillin (about 10 weeks) Is there any relation between the Lactobacillus count and dental caries? Could penicillin therapy be a factor in this high Lactobacillus count?*

G H Starr, Jr, M D, Effingham, Ill

Answer —In more than 80% of cases, high Lactobacillus counts (in excess of 10,000 per cubic centimeter) accompany high caries activity, probably as a result of a high carbohydrate diet and the presence of cavities which provide improved growth conditions for lactobacilli These organisms are no longer considered as the primary bacterial cause of caries Penicillin-containing troches, mouthwashes and dentifrices reduce the counts of lactobacilli and streptococci in the mouth Adequate parenteral dosage has a like effect There is no reason to believe penicillin could contribute to an increased Lactobacillus count in the mouth The large numbers found in the patient in question are probably associated with the frequent eating of sweet carbohydrate foods This might also contribute to the canker or aphthous stomatitis

SEROLOGIC DIAGNOSIS OF SYPHILIS

To the Editor —*A 34-year-old woman developed two small lesions on her face two years ago A biopsy specimen of one lesion was interpreted as Boeck's sarcoid At that time, she had a positive result from the Kolmer-Wassermann test and an equivocal result from the Veneral Disease Research Laboratory test (VDRL) A roentgenogram of her chest showed moderate bilateral hilar adenopathy She gave the following history regarding blood tests in 1942, the result of one test was possibly positive (she was not told the results), and that of another test made by her physician was negative, in 1943, results of a number of tests made by the Navy were negative in some and positive in other instances, in 1945, one result was positive and one negative, and in 1946, 1947, 1950, and 1955 all results were negative*

Results of tests made while I have attended her have been as follows March 27, 1956, Kolmer-Wassermann positive and VDRL doubtful, Feb 3, 1959, Kolmer-Wassermann reactive, VDRL reactive, and quantitative VDRL reactive in two dilutions, April 25, 1959, Treponema pallidum immobilization test (TPI) reactive and spinal fluid showed no red or white blood cells and was negative for globulin, with a total serum protein level of 22 mg%, Wassermann nonreactive and colloidal gold 1110000000, April 4, 1959, Reiter's protein complement fixation test (RPCF) reactive, April 25, 1959, Kolmer-Wassermann reactive, VDRL nonreactive, and RPCF nonreactive, Aug 21, 1959, TPI reactive, Dec 18, 1959, Kolmer-Wassermann positive, VDRL doubtful, and quantitative VDRL positive in one dilution, and Jan 8, 1960, TPI reactive Between September, 1959, and October, 1959, the patient received 8,000,000 units of penicillin intramuscularly in 10 injections

1 Does this patient have syphilis? 2 Does Boeck's sarcoid cause false results from the Kolmer-Wassermann, VDRL, and RPCF tests? 3 Does Boeck's sarcoid or any other condition cause a false-positive result from the TPI test? 4 If this patient has syphilis, would you recommend treatment? 5 If treatment reverses a positive result from the TPI test, how long should it be expected to take? 6 If a person is allergic to penicillin and needs treatment for syphilis, what would be the drug of choice?

M D, Louisiana

Answer —The answers to the five points raised are as follows 1 The presence of syphilis in this patient is established by the repeatedly reactive results of TPI tests The possibility of congenital syphilis should be strongly entertained and careful search made for stigmata Epidemiologic investigation of parents and siblings should be undertaken The basis for suspecting a congenital origin of the patient's infection is that she was only 17 years of age when variable, weakly positive results from serologic tests were first noted, whereas, if the infection had been recently acquired, strongly positive serologic results would have been obtained at that time 2 The precise frequency of biologic false-positive results from the Kolmer-Wassermann or the VDRL test in Boeck's sarcoid is unknown While there is little doubt that this disease may occasionally produce a biologic false-positive result in serologic tests for syphilis, clinical experience has shown that most patients with sarcoidosis who exhibit positive results from serologic tests have syphilis Biologic false-positive RPCF test results apparently do not occur in sarcoidosis 3 Neither Boeck's sarcoid nor any other condition causes a verified false-positive result from a TPI test (barring technical errors) 4 Further treatment for the patient's syphilis is not recommended 5 Treatment cannot be expected to reverse the positive TPI test results in this patient, because the infection was of many years' duration when she was first treated The TPI test can usually be expected to produce a negative result only when patients are treated in the first year of their infection 6 If a patient is allergic to penicillin, treatment with erythromycin or one of the tetracyclines may be administered orally, in a dosage of 2 Gm daily for two to three weeks

CARDIAC PACEMAKER

To THE EDITOR —*I am writing with regard to a question which appeared in* THE JOURNAL, *Aug 22, 1959, page 2174 Having had some experience with the cardiac monitor pacemaker developed by Dr Paul M Zoll of the Beth Israel Hospital, Boston I think that the answer given to the question submitted by Dr Robert L Salb of Crossett, Ark, is misleading Attaching a monitor pacemaker entails no danger whatsoever to the subject, and monitoring can be carried on indefinitely without stimulation and without risk There is no need to stimulate a patient who has normal sinus rhythm No danger is involved in cardiac stimulation during sinus rhythm, but the stimuli are usually painful and are not applied without reason If a patient with normal sinus rhythm is stimulated either intentionally or accidentally, no particular cardiac disturbance results The heart simply responds to either pacemaker, depending on which stimulus arrives in the responsive phase The resulting rhythm may be one of frequent extrasystoles or changing pacemaker, characteristic of parasystole, but no significant disturbance in cardiovascular dynamics results*

The pacemaker is of no value in terminating extrasystoles, tachycardia, flutter, fibrillation, or nodal rhythm It is useful in driving the heart at a faster rate if idioventricular rhythm is too slow External electric countershock with the external defibrillator is indicated to bring about termination of a serious tachycardia that threatens life, such as ventricular fibrillation and possibly ventricular tachycardia, or even supraventricular tachycardia under special circumstances

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TETANUS TREATMENT AND PROPHYLAXIS

To THE EDITOR —*In the Questions and Answers section of* THE JOURNAL, *April 30, page 2132, Edward Shaw, M D, of San Francisco, requested information concerning reports in the medical literature on the use of heparin for the prevention of allergic conditions Although I am not aware of any publication with a title bearing directly on this subject an article suggesting an antiallergic role for heparin, "Heparin and Corticotrophin (ACTH) Analogies and Differences" abstracted in* THE JOURNAL, *Oct 22, 1955, page 822, commented on an antianaphylactic action of heparin Dr Shaw may also be interested in a book entitled "The Mast Cells" which was reviewed in* THE JOURNAL, *Nov 28, 1959 page 1903 One of the items of interest mentioned in the book review was that the mast cells are the site of formation or storage of heparin, as well as being the site of origin of histamine*

From time to time I hear criticism of THE JOURNAL *of the American Medical Association, allegedly because it makes no significant contribution to the medical literature It has been my own personal experience that* THE JOURNAL *constitutes an amazing storehouse of medical information of all kinds, for those who take the trouble to study it and store the information, properly indexed, so that it can be readily retrieved*

Finally, I would like to refer Dr Shaw to a fellow San Franciscan, Milton M Hartman, M D 450 Sutter St, who has been in communication with me in the past, relative to material he has available for presentation at medical meetings on the use of heparin in allergic disturbances Hartman reported on the role of heparin in allergic conditions (Am J Med 21 85 *[July] 1956) In more recent publications on the mechanism of the acute allergic reaction* (Journal Lancet 79 274 *[June] 1959,* A M A J Dis Child 97 163 *[Feb] 1959), reference can be found to the role of heparin in allergic reactions*

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ABSTRACTS FROM THE LITERATURE

Archives of Internal Medicine

106 172-260 (Aug) 1960

Urine Electrophoresis in Patients with Multiple Myeloma
H H Zinneman H Olenchur and D F Gleason p 172
Use of Vancomycin, Ristocetin and Kanamycin
B A Waisbren and others p 179
Evaluation of I^{131} Therapy in Graves Disease
J Domnitz H P Hurd and J W Goldzieher p 194
Retinopathy in Treated Malignant Hypertension
G Lockhart and others p 205
Role of Splenectomy in Sarcoidosis
J Bertino and R M Myerson p 213
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Turban Tumor
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Hemorrhage from Leiomyomas of Gastrointestinal Tract
B F Huntley A R Laurain and W H Stephenson p 245
Cystic Fibrosis of the Pancreas
R W Trever and I W Abrahams p 253

Urine Electrophoresis and Multiple Myeloma —The results of simultaneous electrophoresis of serum and urine in 37 myelomatous patients were evaluated and correlated with necropsy findings when available Twenty-eight patients had a characteristic paraprotein peak in the serum, 6 also had Bence Jones proteins in the urine Nine patients did not have a paraprotein peak in the electrophoretic pattern of the serum all excreted Bence Jones proteins in the urine At autopsy characteristic hard protein casts of the myelomatous kidney were found only in the renal tubules of those patients who had excreted Bence Jones proteins during life The urine of 3 patients of the 1st group contained all of the major serum protein fractions in the urine At necropsy 1 proved to have amyloidosis with extensive glomerular involvement Twenty to 25% of all myeloma patients do not have characteristic paraprotein peaks in the serum and would escape early diagnosis by serum electrophoresis alone Since this very group of patients has Bence Jones proteinuria in nearly every instance, electrophoresis of serum and urine will afford a correct and early diagnosis Appearance of all major serum protein fractions in the urine signifies amyloidosis with involvement of the renal glomeruli

Use of Vancomycin, Ristocetin, and Kanamycin —Ristocetin, vancomycin and kanamycin were administered alternately to 131 patients with severe staphylococcic infections or bacterial endocarditis The groups of patients receiving each drug were found to be comparable and the relative clinical effectiveness and toxicity of the 3 drugs were determined Each drug was effective in slightly over one third of the patients studied No one antibiotic showed marked clinical superiority over the others Significant ototoxicity and nephrotoxicity were found with ristocetin, kanamycin and vancomycin In addition, ristocetin caused a high incidence of skin reactions and caused depression of the granulocytic series of white blood cells in some patients The conclusion was reached that ristocetin, kanamycin and vancomycin are effective antistaphylococcal agents of approximately comparable activity They all exhibit toxicity greater than that found with the tetracyclines, penicillin, and chloramphenicol Therefore, ristocetin, vancomycin and kanamycin should be used only in cases that have not or are not likely to respond to safer antibiotics and in which the condition of the patient justifies the risk of serious toxic reactions

Retinopathy in Treated Malignant Hypertension —This report describes the retinopathy of 96 patients with malignant hypertension before and during antihypertensive drug treatment These patients were divided into 2 groups group 1 those who died of progressive arteriolar disease or atherosclerotic complications, and group 2, those who have survived Prior to treatment, group 1 differed from group 2 by having more papilledema and greater numbers of exudates, arteriolar constriction, sclerosis, and number of hemorrhages were the same in both groups The increased severity of retinopathy in group 1 reflected the over-all greater severity of vascular disease in this group as compared to that of group 2, but could not be correlated with the severity of renal disease Adequate antihypertensive treatment not only controlled the extraretinal signs of vascular disease but was associated with disappearance of hemorrhages, exudates, and papilledema, even in those patients with poor blood pressure control, these retinal abnormalities improved considerably Treatment did not change arteriolar constriction and sclerosis This experience suggests that treatment controls but does not cure the underlying vascular disease

Role of Splenectomy in Sarcoidosis —Although involvement of the spleen occurs frequently in sarcoidosis, sequelae of splenic sarcoidosis are rarely seen When present, they may take the form of either anatomical or functional complications The former include rupture and abdominal discomfort, the latter hypersplenism Hypersplenism due to sarcoidosis may be manifested by neutropenia, thrombocytopenia or anemia, occurring either singly or in combination The difficulty that may be encountered in obtaining a preoperative diagnosis is illustrated by the 2 cases presented Both patients had marked splenomegaly and pancytopenia Splenectomy was performed in both, with immediate improvement in the blood picture Improvement has been maintained in both patients for over 4 years

Accidental Hypothermia —Eight cases of accidental hypothermia due to exposure were treated at Albany Hospital during the years 1946 through 1958 These cases have been reviewed with respect to admission clinical data, laboratory findings, clinical course and autopsy findings A brief summary of the physiological changes occurring in the temperature range of 75 to 90 F (24 to 32 C) has been presented and correlated with the clinical findings The complications occurring during the rewarming period have been discussed, including frostbite and gangrene pneumonia, arrythmias, hyper-reactivity to heparin, gastrointestinal bleeding with or without perforation, oliguria, edema, and hypotension Comments on therapy and management have been presented which it is hoped, may help to reduce the mortality of 87 5% shown in this series Two illustrative case reports are included

Induced Sputum as Diagnostic Technique—The technique of mobilizing sputum for the diagnosis of lung cancer was significantly improved by heating inhaled aerosol to 125 F (51 7 C), the fall in its temperature to 98 F (36 7 C) in the respiratory tract resulted in condensation of aerosol solution and water vapor This effect was enhanced by the 4-fold increase in the amount of solution nebulized Cytological examination revealed better-preserved cellular morphology in induced than in spontaneous sputum In 42 cases, there was 1 unsatisfactory specimen and no false positive In 14 cases of suspected malignancy, the induced sputum was satisfactory in all and a positive diagnosis was made in 9 Of the spontaneous specimens, a positive diagnosis was made in 2 Of 6 spontaneous specimens reported as negative, the results of induced sputum were reported as positive in 3 and suggestive of abnormal cells in the remaining 3 Studies were initiated on the effect of gases of increased density, such as sulfur hexafluoride (SF_6), in respect to enhancement of the effectiveness of coughing

Meprobamate Overdosage—Meprobamate's recent popularity has placed it in a position to be used as a suicide vehicle by the depressed patient Eight patients with meprobamate overdosage were seen in a 12-month period at the St Vincent's Hospital of the City of New York Five of these patients are reported in detail A consistent clinical picture was observed The outstanding features were severe hypotension without loss of response to painful stimuli or loss of deep tendon reflexes Respiratory function was not significantly disturbed Hypotension is stressed as the main therapeutic challenge The importance of constant observation of vital signs during the comatose interval is indicated since hypotension may develop at any time during this period All of the patients were successfully managed with vasopressors Analeptics and antibiotics were not used

Turban Tumor—Turban tumor is a benign, usually multiple, tumor with a predilection for the scalp Beginning at or after puberty, slow-growing rubbery sessile or pedunculated tumors may eventually cover the entire scalp like a turban The tumors may occur elsewhere on the skin, especially the back or chest, as single or multiple lesions Histologically they consist of epithelial cell masses separated by connective tissue which tends to degenerate into wide homogeneous pink staining strands They are believed to be derived as cutaneous appendages from the embryonal stratum germinativum and to be related to apocrine glands They resemble Von Recklinghausen's neurofibromatosis but are firmer and usually confined to the scalp They are more pedunculated than sebaceous cysts or wens Treatment is surgical excision

Hemorrhage From Leiomyomas—Six patients with smooth muscle tumors of the gastrointestinal tract are reported These cases illustrate the peculiar tendency of leiomyomas to produce recurrent massive gastrointestinal bleeding Benign tumors, at times as small as 2 cm in diameter, may be associated with episodes of exsanguinating hemorrhage over a period of months or years These tumors tend to be attached to the stomach or intestinal wall by a small pedicle and to extend as mobile masses into the peritoneal cavity Because of their predominately extramucosal growth they are often difficult to demonstrate by x-ray Repeated acute bouts of gastrointestinal bleeding with negative x-rays should suggest the presence of these tumors, and early exploration should be carried out since fatal hemorrhages have occurred from small benign leiomyomas

Cystic Fibrosis of the Pancreas—Prolonged survival in cystic fibrosis of the pancreas is no longer a rarity In a review of 67 patients with this disorder seen at the Johns Hopkins Hospital survival beyond the age of 14 years was documented in 6 instances Characteristic features of the disease in these older patients included rather severe manifestations of chronic pulmonary infection (bronchiectasis and recurrent pneumonia), pulmonary fibrosis and emphysema, and cor pulmonale with flare-ups of respiratory infection Pansinusitis was almost always present Symptoms of malabsorption were minimal

Archives of Otolaryngology

72 147-226 (Aug) 1960

Otosclerosis with Bilateral Stapes Mobilization
F Altmann M Basek, and J V Hough p 14
Viral Pneumonia in the Mother and Hemorrhagic Otitis in Fetus
G Kelemen and J H Neame p 163
Cephalic Tetanus
L J Rutledge, E T Krementz, and H E Kellum Jr p 170
Anesthesia for Tonsillectomy Without Ether or Endotracheal Tube
S M Shane and others p 178
Facility in Tonsilloadenoidectomy Management
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An Operative Method in Treatment of Ozena
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Cancer of the Pyriform Sinus
P M Brown and K D Devine p 192
External Dacryocystorhinostomy
R L Pulham p 194
Congenital Dehiscence of Fallopian Canal in Middle Ear Surgery
J Kaplan p 19
Middle Ear Muscle Reflex in Auditory Research
H B Perlman p 201
Observations on Neurochronaxic Theory of Voice Production
H J Rubin p 20
Alloplastic Materials in Creation of Facial Contour
B B Rish p 212
Cervical Chordoma Diagnosis and Operation
H Foole and D Ioannovich p 219

Facility in Tonsilloadenoidectomy Management—Some knowledge to facilitate tonsilloadenoidectomy (T&A) management was gained from 2400 cases Written instructions were given to patients to explain the surgical course and the use of medications including vitamin K, C and B mixture, antibiotics (usually penicillin) for 10 days' coverage, and carbazochrome salicylate (Adrenosem) for oozing in the recovery room Delayed hemorrhage (after 24 hours) using the above routine was 0 63%, immediate hemorrhage (first 24 hours) was considered to be much higher (3 or 4%) A 400-case series was used as a special study, 200 preoperatively received conjugated estrogenic substance (Premarin) intramuscularly, 200 did not The latter had 2 5% bleeders those receiving conjugated estrogenic substance had only 1%

External Dacryocystorhinostomy—The purpose of this paper is to reacquaint the profession with the value of the Dupuy-Dutemps procedure Modifications of this operation consist of (1) the wide removal of the bone for a distance of 2 5 cm in the region of the lacrimal bone and (2) the formation of anterior and posterior flaps of the nasal mucosa which are sutured to the medial wall of the lacrimal sac This direct suture plus the preservation of the medial wall of the lacrimal sac will prevent the formation of scar tissue which so often obstructs the new intranasal opening when other techniques of dacryocystorhinostomy are used The postoperative care is minimal Good results were obtained in better than 90% in this series of 28 patients This technique is simpler and will give better results with less postoperative care than the intranasal procedures

Congenital Dehiscence of Fallopian Canal—In a series of 100 consecutive stapes mobilization approaches the horizontal portion of the (intratympanic) fallopian canal was carefully inspected and palpated under 16× magnification using the Zeiss operating microscope. All cases of inflammatory nature were excluded, only cases of otosclerosis diagnosed otologically and audiometrically and verified at surgery were used in the series. Gentle palpation with a blunt-tipped instrument such as the Derlacki mobilizer causes the mucoperiosteum and the exposed facial nerve adjacent to the stapedial footplate, to quiver characteristically. There were 7 cases of dehiscence of the fallopian canal in this series. This not common finding assumes importance because of the present use of bolder footplate manipulations. Developmentally, the fault may be explained by the course of the embryonal stapedial artery persisting past the 3rd fetal month and leaving the aperture in the facial nerve canal as a dehiscence in adult life.

Middle Ear Muscle Reflex in Auditory Research—The difference in the threshold of the acoustic middle ear muscle reflex and that of acoustic sensation is 40 to 100 db, depending on the method of observation. Peak tension to a sustained tone is rapidly developed but not maintained. Reduction or abolition of contraction to very loud sounds may be frequency dependent. Masking of sounds does not decrease the contraction. The threshold of auditory sensation is not changed by cutting or paralyzing the muscle. Only sounds of intensity corresponding to the threshold of reflex contraction are heard louder or produce more damage in the unmuscled ear. The speed of contraction is too slow to protect the ear from brief intense noise (i.e., blast), but the contracting muscles impair the response of the middle ear to low frequencies. Despite all this information the physiological role of the muscles remains obscure.

Alloplastic Materials in Creation of Facial Contour—This work represents a 9 year study in which a total of 76 acrylic chin implants have been buried for the cosmetic restoration of facial contour. It illustrates the technique for implantation and details by histological studies the absence of reaction to this specially prepared material. It also points out the important fact that not 1 single complication has occurred either in the form of extrusion or infection. Additional surgical procedures, which most patients will not welcome such as obtaining iliac bone or costal cartilage, are completely obviated by the simple use of these prepared chin implants which are available in several predeterminized sizes. The incidence of absorption is, of course, nil. This study emphasizes the importance of complete facial restoration or profile plasty, and illustrates the excellent results which are gratifying to both the physician and the patient.

Cervical Chordoma Diagnosis and Operation—Cases of chordomas are rare in this country. Only 12 histologically confirmed ones have been reported by Greek authors. We add our case concerning a cervical chordoma in a female white patient, aged 42, preoperatively diagnosed at biopsy. The tumor was localized at the left of the hypopharynx originating from the C_3 C_4 vertebrae. The neck was free of ganglions or swelling. The x-ray examination showed destruction of some osseous trabeculae of the body of the C_3 vertebrae. The biopsy revealed a chordoma not presenting characters of malignancy. The tumor was successfully removed by the lateral cervical route. Prognosis cannot be established without any reserve for the future. On this occasion we review the literature and discuss embryological, statistical, diagnostic, and therapeutic viewpoints regarding chordomas.

Alabama State Med Assn Journal, Montgomery

29 413-472 (May) 1960 Partial Index

Perforation of Infarcted Interventricular Septum
J F Crenshaw and L L Campbell p 419
Cerebral Claudication
J M Cameron and H J Till p 424

Perforation of Infarcted Interventricular Septum—The authors report a 53 year-old woman in whom diagnosis of perforation of the infarcted interventricular septum was made before death. Diagnosis of this complication is not difficult if this entity is kept in mind. Following an acute myocardial infarction a sudden change for the worse in the patient's general condition, the onset of a loud, blowing, low-pitched systolic murmur along the lower left sternal border is highly suggestive of septal perforation. The differential diagnosis is discussed, emphasis being placed upon differentiation from the rupture of a papillary muscle. The prognosis is poor. Medical treatment is unsatisfactory. Surgical treatment holds some degree of promise for the future.

American Heart Journal, St Louis

59 643 802 (May) 1960 Partial Index

The Electrocardiogram in Tetralogy of Fallot
F Pileggi and others p 667
Chronic Pernicious Myocarditis
I K Kline and O Saphir p 681
The Jugular Venous Tracing
H Hartman p 698
A New Coronary Vasodilator
G Sandler p 718

Electrocardiogram in Tetralogy of Fallot—The authors studied the electrocardiograms obtained from 142 patients with tetralogy of Fallot at the Hospital das Clinicas of the University of São Paulo, Brazil, in order to determine the diagnostic value of a standard electrocardiographic pattern in this combination of congenital cardiac defects, and to ascertain whether there is any difference between the electrocardiograms of the 2 main hemodynamic types of this malformation, one with right-to-left and the other with left-to-right shunt. This study was made from both the scalar and the rectonal electrocardiographic points of view. The results justify the conclusion that in most patients with tetralogy of Fallot the electrocardiogram shows a uniform behavior which relates to the hemodynamic picture. When in a patient with tetralogy of Fallot a qR, qRs or qRS pattern with a delayed intrinsicoid deflection is registered in leads V_5 and V_6 one can make the diagnosis of an associated left ventricular enlargement which might be related to an arteriovenous shunt through the interventricular septal defect, so-called atypical Fallot. The presence of qR patterns in the right precordial leads in patients with tetralogy of Fallot associated with marked cardiomegaly and evident enlargement of the right auricle has been emphasized.

Chronic Pernicious Myocarditis—Of 2,625 patients who died in hospital in Chicago and on whom autopsies were performed, myocarditis was observed in 225 (8.4%), among these 6 between the ages of 8 and 50 years were reclassified as having had chronic pernicious myocarditis These 6 patients had severe myocardial insufficiency over a prolonged period of time, with a protracted, relentless, downhill course culminating in death An erroneous diagnosis of stenosis of the mitral orifice had been made in 2, and of pericarditis in 1 At autopsy, in all 6 patients a large heart was found, with no changes in the endocardium or pericardium On microscopic examination there was a true chronic, mainly interstitial, myocarditis with young connective tissue compressing and eventually replacing heart muscle fibers, and an interstitial infiltration of inflammatory cells The importance of recognizing pernicious myocarditis lies principally in its grave prognosis After a seeming recovery from a slowly developed illness which may or may not be recognized as myocarditis, the patients show signs and symptoms of early myocardial failure Once this happens, it is bound to recur These are the patients who either become cardiac invalids or recover only to have repeated attacks of myocardial decompensation and to succumb to 1 of them This realization is implied in the term "pernicious" myocarditis This type of myocarditis is in no way a specific anatomic entity, and any chronic myocarditis occasionally may cause a protracted and relentless downhill course From observations made on the 6 patients and from the study of the pertinent literature, it appears that in the geographic region of the United States a chronic form of isolated myocarditis is the most common cause

American Rev Respiratory Diseases, New York

81 643-804 (May) 1960 Partial Index

Mass Chemoprophylaxis of Tuberculosis
E Groth-Petersen U Gad, and F Østergaard p 643
Pleuropulmonary Amebiasis Analysis of 10 Cases
B H Webster p 683
Pulmonary Histoplasmosis Pneumoperitoneum Therapy
A Saliba, O A Beatty and A Pakalns p 709
Rapid Mouse Test for Diagnosing Pulmonary Tuberculosis
D Gale and E A Lockhart p 715

Pleuropulmonary Amebiasis —The 10 cases of pleuropulmonary amebiasis presented were observed in a series of 249 cases of amebiasis (4 02%) Nine of the 10 patients with the pleuropulmonary form of amebiasis belonged to the group of 48 patients with hepatic amebiasis, and 1 patient had an amebic bronchitis without demonstrable liver involvement The diagnoses in the 10 patients were substantiated by the demonstration of Entamoeba histolytica in the sputum in the form of trophozoites in 9 cases and as cysts in 1 case A bronchobiliary communication existed in 8 of the patients None of the 10 had ever been outside the continental United States, only 4 had had frank dysentery, 1 person lived in a rural area The ages of the patients ranged from 36 to 82 years Some drugs are effective against the Entamoeba histolytica in the intestinal tract, whereas others attack the protozoa that have invaded the tissues Since some extraintestinal amebic invasion probably exists in a large percentage of amebic infections, drugs with various types of action should be employed In 6 of the 10 patients treatment consisted of chloroquine alone or in combination with other drugs Diiodohydroxyquinoline glycolylarsanilate (Triamar) was successfully used in 3 cases Emetine hydrochloride was employed in only 1 case A drug to combat the intestinal organisms was thought to be necessary in each case Other antimicrobials were employed when an associated bacterial infection was thought to be present

Mouse Test for Diagnosing Pulmonary Tuberculosis —Whereas the culture methods ordinarily used to ascertain whether a patient is discharging viable tubercle bacilli require 3 to 4 weeks for a positive and 6 to 8 weeks for a negative result, the mouse test evaluated in this paper may reveal a positive result in 5 days Four mice per sediment are inoculated intraperitoneally One mouse in each group is sacrificed at 5, 10, 15 and 20 days, respectively A total of 1,012 specimens from 362 patients were studied The patients included 188 from tuberculosis treatment wards, 55 from medical wards and 119 from out-patient services The last 2 groups were to serve as controls The mouse test was not only more rapid, but was also more sensitive than the usual culture procedures for the detection of tubercle bacilli Of the 362 patients in the study, 145 patients (40%) yielded specimens which were positive by the mouse test in 20 days, whereas the specimens from 75 patients (20%) were positive by culture in 52 days Of the 75 patients whose specimens were positive by culture, 84% gave positive results by mouse test in 5 days and 96% in 10 days, whereas no cultures were positive in 10 days

American Journal of Medical Sciences, Philadelphia

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A Lattimer, A J Simon and M H Lepper p 548
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R J T Joy and W R Beisel p 601
Reticuloendothelial System in Hurler s Disease
L F Jermain R J Rohn, and W H Bond p 612

Circulatory Action of Nylidrin Hydrochloride —The authors studied 25 patients, 30 to 74 years of age, with arteriosclerosis involving the lower extremities who had intermittent claudication and other symptoms of ischemia of the limbs, such as night pain, 5 of these patients had lightheadedness or vertigo, mental confusion or diplopia, and murmurs over the carotid arteries or other evidence of cerebral vascular insufficiency All the patients were given 5 mg of nylidrin hydrochloride intramuscularly or intravenously In addition, 20 patients were given 6 mg of the drug, 3 times daily, by mouth Additional studies were carried out on 11 rabbits The results showed that the patients tolerated the drug well In the experimental animals and in the patients nylidrin hydrochloride increased the blood flow in the muscle of the calf and in the brain, and to a minimal extent in the fingers and toes There was also an increase in cardiac output (minute volume and stroke volume) The drug produced symptomatic clinical improvement when used in the management of cerebral vascular insufficiency and ischemic leg night pain

Reticuloendothelial System in Hurler's Disease —Single or multiple bone marrow specimens were obtained from 12 patients, 4 months to 16 years of age, with Hurler's disease The study of these specimens revealed the invariable presence of phagocytic clasmatocytes containing inclusions These inclusions seem to be unique to this disorder The inclusions varied widely in size and shape, but consisted of a central staining body and a peripheral unstained clear zone They were occasionally observed in plasma cells and, in 1 patient only in the lymphocytes monocytes and neutrophilic granulocytes This was the only patient in this series showing the Alder body phenomenon The central staining body proved by differential histochemical staining to be a mucopolysaccharide, but the authors studies failed to define the constituents of the peripheral clear zone An attempt was made to demonstrate such Hurler s cells in the bone marrow of the clinically unaffected mother, father, or sibling of 1 of these patients with Hurler s disease, but none could be found The appearance of these cells in the bone marrow would seem to antedate the appearance of other manifestations of this disorder

Beitrage zur Klinik der Tuberkulose, Berlin

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Pneumonectomy on Children and Juveniles —Of 107 pulmonary resections performed at a children s sanatorium, 7 (6 5%) were *pneumonectomies* to which 3 boys and 4 girls between the ages of 7 and 19 years were subjected Pneumonectomy was indicated from the beginning in 5 patients in 3 of whom 1 lung was destroyed and in 2 because of cavitary tuberculosis of upper lobe extensive bronchial tuberculosis, and bronchiectasis of lower lobe The clinical diagnosis corresponded with the morphologic findings which confirmed the indications in these 5 patients In the remaining 2 patients a lobectomy was 1st planned but because of anatomic peculiarities the entire lung had to be removed It is obvious that each resection should be performed only according to the most exact indications In patients with bilateral disease one should also consider intrapleural or extrapleural pneumothorax As a rule the patients tolerated the pneumonectomies well

British Medical Journal, London

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R F Fouche J R Spears and C Ogilvie	p 1312
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Treatment of Simple Hirsutism —The authors treated 21 women with simple hirsutism and 3 women with the hirsute type of Stein-Leventhal syndrome by the administration of prednisone at St Thomas s Hospital, London The drug was usually given in doses of 10 mg per day and usually combined with ethinyl estradiol The 3 patients with the Stein-Leventhal syndrome were given steroid therapy after menstruation had returned to normal as a result of ovarian wedge resection, to which 7 additional patients with this syndrome were subjected but were not treated with prednisone In 6 of the 24 patients treated with prednisone there appeared to be significant improvement, but improvement was doubtful in an additional 9 Of six patients with Stein-Leventhal syndrome who had been operated on, 4 became pregnant within 6 months after the operation While steroid therapy may benefit the occasional patient to a noticeable degree when a reasonably low dosage level is used, the authors do not feel that it is sufficiently beneficial to justify its routine use It is not yet possible to predict whether any particular person will respond, and the problem of relapse on cessation of treatment also arises

Treatment of Tuberculous Meningitis —The author reports on 210 children with tuberculous meningitis who were treated at a children s hospital, between 1947 and 1958 Of these 131 (65%) survived and 105 (50%) have no neurological or mental sequelae In the course of the 12 years the results progressively improved with increased experience in management and with the introduction of aminosalicylic acid (PAS) followed by isoniazid as specific antituberculosis drugs and purified protein derivatives (tuberculin) and corticosteroids as adjuvants Since the introduction of isoniazid, 66 (83%) of 80 children survived, and 55 of them have no sequelae The most difficult patients were those who were less than 3 years of age and were unconscious on admission, none of those, so far, have made a complete recovery Intrathecal administration of streptomycin has not been abandoned, but the minimum course is now reduced to 10 injections in doses of 20 to 50 mg per injection The present routine treatment consists of a minimum 6-month course of isoniazid given by mouth in divided doses of 20 mg per kilogram of body weight daily together with 40 mg of streptomycin per kilogram given intramuscularly in a single daily dose PAS is given initially and is continued for 6 months if there are no side effects During most of the 6-month course the children are ambulant and either are treated at home or receive regular schooling in hospital Cortisone is now administered systematically to all children who are less than 1 year old or who are unconscious on admission Hydrocortisone given intrathecally in doses of 10 to 25 mg is of value in threatened or established spinal block

Canadian Medical Association Journal, Toronto

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Allergic Reactions to Antitetanus Serum —The question is raised whether allergic reactions to the prophylactic administration of antitetanus serum (ATS) cause more morbidity and deaths in Canada than the tetanus which the serum is intended to prevent About 7,900 severe allergic reactions to ATS occur annually in Canada but no definite figures are available on the number of deaths caused by these reactions One of the 2 fatal anaphylactic reactions described by the author resulted from an ATS skin test, this was a typical instance of the atopic type of horse serum allergy The 2nd patient received 1,500 units of ATS after a scratch test with ATS had proved negative Generalized urticaria developed 7 days later, coma developed on the 8th day The patient died on the 13th day without recovering consciousness Postmortem examination revealed acute necrotizing hemorrhagic encephalopathy This seems to be an example of the acquired type of horse serum allergy, which is rare and unpredictable Three things are essential to reduce the morbid reactions and deaths from the use of ATS (1) Less ATS must be given, (2) as many persons as possible should be immunized with tetanus toxoid, (3) a permanent record should be kept of this immunization, preferably in a central registry With regard to point (2) the author feels that the more persons who are actively immunized against tetanus, the fewer there will be who will require ATS The protection against tetanus conferred by immunization with toxoid is more efficient and longer lasting than that conferred by ATS The practical importance of point (3) will be obvious to anyone who confronts this problem of tetanus prophylaxis in his day-to-day practice

Surgical Treatment of Parkinsonism—The authors summarize their experiences of the past 6 years in the surgical treatment of paralysis agitans (parkinsonism or Parkinson's disease) Most of the 100 patients with Parkinson's disease reviewed for this report were operated on in the following manner With the help of a so-called pneumotaxic guide, the center of the foramen of Munro was brought in line with the central ray of a standard craniograph Stimulation and recording were then carried out at a point situated about 10 mm below and behind the center of the foramen of Munro at 15 mm from the midline of the 3rd ventricle Finally, a section was made with a fine wire leukotome placed immediately above and in front of the point for low voltage motor-face stimulation Such surgical lesions have produced marked improvement in more than 80% of cases presenting tremor, rigidity, or akinesia The remission obtained was doubtful in less than 5% of the patients Chief contraindications to the procedure are mental alterations or severe organic disease Bilateral procedures should be used selectively and only in mentally alert patients While surgery may not be the final answer to Parkinson's disease, patients are greatly helped by careful, well-localized surgical lesions Harmful results from accurate section are minimal

Chirurg, Berlin

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Urgent Surgery for Diaphragmatic Hernia in Infants F Kummerle	p 169
Phemister s Bone Splint Plastic Possibilities and Results K Blanke and W Hiemsch	p 172
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Surgery for Diaphragmatic Hernia in Infants—The life of newborn infants with diaphragmatic hernia is often threatened by cardiorespiratory disturbances during the 1st hours or days after delivery After they have survived for a month, the threat to survival is lessened, but then there may be intermittent gastrointestinal disturbances with symptoms of ileus Sometimes congenital diaphragmatic hernia is not recognized until autopsy, a mortality of 75% has been reported for infants with untreated diaphragmatic hernia The author mentions the different forms of diaphragmatic hernia, or prolapse, and reviews observations on 5 infants (ranging in age from 36 hours to 11 months) who were treated at the Surgical Clinic of the University of Freiburg in the last 4 years Three of the 5 infants had pleuroperitoneal prolapse and 2 had subcosto-sternal hernias Two especially interesting cases are described One of these 2 infants, operated on 36 hours after delivery, had a diaphragmatic hernia on the left side with enterothorax Another infant, operated on when 4 weeks old, had a subcostosternal hernia with prolapse of the right lobe of the liver into the thorax The symptoms of diaphragmatic hernia are determined by the size and position of the hernial aperture, by the type and extent of the prolapsed viscera, and by their mechanical and functional effect on the thoracic organs Roentgenoscopy at 2 levels generally will explain the clinical symptoms None of these 5 infants died The use of an intubator proved valuable during the postoperative treatment Although some reports indicate rather high surgical mortality, it is never as high as the death rate of untreated infants with diaphragmatic hernia

Pseudopheochromocytoma—The author presents 2 cases of pseudopheochromocytoma observed at the University Clinic, Berlin A 66-year-old woman had been subject to fainting spells for many years, but latterly she had had attacks of palpitation and sweating during which the blood pressure increased to 280/120 mm Hg, whereas generally her blood pressure was 160/80 mm Hg Pyelography revealed a space-infringing process in the left kidney Examination of the retroperitoneum suggested hyperplasia of the left adrenal gland The intravenous injection of regitine promptly counteracted a sudden increase in blood pressure, and, whereas the histamine test was positive for pheochromocytoma, the cold-pressure test gave only a suggestion of positivity, there being no increase in the diastolic value Surgery revealed an intrarenal cyst the size of a hen's egg, which caused pressure atrophy of the renal tissue No changes were noted on the adrenal gland The left kidney was removed by nephrectomy Histological examination of the surgical specimen revealed, in addition to the renal cyst, pyelonephritis and arteriosclerosis There were no further blood pressure crises during the follow-up period In the 2nd patient the symptoms of pheochromocytoma subsided after removal of a renal cyst The author points out that in 1959 Hradec and Pacovsky reported several patients in whom, although they had the symptoms of pheochromocytoma, no tumor of the chromaffin tissue could be found but local lesions were found in 1 or both kidneys The conclusion is reached that the regitine, histamine, and cold pressure tests do not suffice for the diagnosis of pheochromocytoma, but an increase in the urinary excretion of the catechol amines must be demonstrated as well

Geburtshilfe und Frauenheilkunde, Stuttgart

20 313-416 (April) 1960 Partial Index

Carcinoma of Uterine Cervix in Pregnancy W Bickenbach and H J Soost	p 313
Pelvic Calcifications in Genital Tuberculosis P Drobnjak M Bačic and B Mark	p 365
Diagnosis and Prognosis of Carcinoma of Cervix H Lau and M Stork	p 383

Carcinoma of Uterine Cervix in Pregnancy —The authors report on 28 pregnant women who were treated for carcinoma of the uterine cervix at the 1st gynecologic clinic of the University in Munich From a comparison of the results obtained in these patients with those reported on by other workers conclusions are drawn as follows (1) Early diagnosis is very important because prognosis is good during pregnancy, becomes worse towards the end of pregnancy, and becomes definitely poor postpartum (2) Treatment should be instituted immediately after the diagnosis has been made, regardless of the state of pregnancy (3) Only after the 28th week should attempts be made to preserve pregnancy in order to obtain a viable infant The authors experiences and those of other workers suggest that during pregnancy the same good results may be obtained with irradiation therapy as with surgical treatment This definitely applies to early pregnancy, and probably also to the later months of pregnancy To avoid a situation definitely unfavorable to the successful treatment of the carcinoma postpartum or after abortion seems to be more important than the decision whether to operate or to apply radiotherapy The authors attempt to accomplish this by artificially maintaining a state similar to pregnancy by hormonal substitution for a short period after the termination of radiotherapy

German Medical Monthly, Stuttgart

5 73-112 (March) 1960 Partial Index

Ventricular Aneurysms or Diverticula Surgical Treatment
E Derra and F Loogen p 77
Relationship Between Fatty Liver and Diabetes Mellitus
H Kalk p 81
Growing Incidence of Severe Congenital Abnormalities
B de Rudder p 84

Fatty Liver and Diabetes Mellitus —It was found that the coexistence of diabetes and cirrhosis far exceeded the expected fortuitous association The author, who performed liver biopsies in 170 diabetic patients reviewed the histological findings in 121 of these and compared the findings with other clinical data Cirrhosis of the liver was histologically demonstrated in 39 of the 121 patients In 18 patients diabetes preceded cirrhosis, while in 16 patients cirrhosis or hepatitis preceded the onset of diabetes It is thought that in the latter group hepatitis and the subsequent cirrhosis led to pancreatic disease A high percentage of patients in whom diabetes develops at a mature age have fatty liver There were 49 such cases (40%) among the 121 diabetic patients Fatty liver in conditions other than diabetes has been known to be followed by cirrhosis, histological study showed the same changes in the fatty liver of diabetic patients There are coarse fat droplets prominent vacuolization, lighter color, and variation in size of the liver-cell nuclei This picture was also seen in those patients in whom diabetes did not develop until later, that is there exists a prediabetic stage in which a still compensated defect in the carbohydrate metabolism leads to fatty liver changes Not only could the development of diabetes be predicted from the histological picture, it was also possible to prevent the development of diabetes by a low-calorie and low-carbohydrate diet and by abstinence from alcohol

J Thoracic & Cardiovas Surgery, St Louis

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Radical Lobectomy
W C Cahan p 555
Pyogenic Pulmonary Abscess Prognosis and Treatment
M N Andersen and K E McDonald p 573
Anteriorly Crushed Chest or Steering-Wheel Injury
M Virshup p 579
Aberrant Left Pulmonary Artery and Respiratory Obstruction
J H Jacobson II and others p 602
System for Hypothermic Perfusion
N Zuhdi and others p 629
Differentiation of Aneurysm and Mediastinal Tumor
J E Connolly and others p 640
Plication of the Aortic Ring in Aortic Insufficiency
E S Hurwitt P W Hoffert and A Rosenblatt p 654
Mitral Commissurotomy in Pregnancy 37 Cases
A M Dogliotti and others p 663

Radical Lobectomy —In a radical lobectomy 1 or 2 lobes of a lung are excised in a block dissection together with certain of the regional hilar and mediastinal lymph nodes, whereas in simple lobectomy the regional lymph nodes are not removed Autopsy evidence that lymph nodes are the most frequent sites of metastases from lung cancer has been confirmed by studies on lymph nodes removed in the course of radical lobectomies or pneumonectomies Lymph-node metastases are likely to exist regardless of size, position, or histologic type of the primary tumor The description of the technique of the radical lobectomy is illustrated by diagrams and the author discusses the clinical implications of radical lobectomy on the basis of observations in 48 such operations performed on the Thoracic Surgical Service of Memorial Center, New York, from 1951 to 1958 Thirty-four of the radical lobectomies were performed for primary lung cancers, 9 for metastases in the lung, and 5 for benign, tumor-like conditions Hilar and mediastinal lymph-node metastases were found in 41 5% of the patients who were subjected to radical lobectomy Of 8 patients who so far have survived 5 or more years, 5 had invasion of lymph nodes at the time of operation and 3 of these are now free from evidence of disease The extensive resection of the involved lymph nodes is believed to be largely responsible for this long survival The pathologic study of these lymph nodes, together with the knowledge of the histology of the primary cancer, and evidence of blood vessel invasion by tumor are 3 essential aids in forecasting survival

Pyogenic Pulmonary Abscess —Since the advent of antibiotics acute bacterial pneumonitis is often aborted and empyema and abscesses develop less frequently, but there are still some patients who fail to respond to antibiotics and either die or require surgery In order to identify helpful prognostic factors, the authors reviewed the histories of 90 patients with primary pyogenic pulmonary abscess treated during the 10-year period prior to 1959 Sixty per cent of the patients were over 50 years of age, and most of them were from a low economic stratum or were indigents Poor oral hygiene has frequently been incriminated, and in this group of 90 patients 63 had carious teeth and 11 were edentulous In 20 patients the abscess developed after acute bacterial pneumonitis A possible source of aspiration existed in 9 patients, 4 had had dental extractions, 2 had undergone tonsillectomy, 2 had had alcoholic bouts with stupor and emesis, and 1 patient had had a purulent sinusitis Four patients had had a cerebrovascular accident with coma and 4 had chronic epilepsy, conditions that may also predispose to aspiration The medical therapy consisted of the use of antibiotics, postural drainage, and supportive measures It was effective in 31 patients, while 21 died and 38 required operation The abscess was the chief cause of death in 11 of the 21 fatalities, these patients might have been cured with more effective treatment of the abscess The other 10 succumbed to associated diseases Failure of cure by medical therapy alone is indicated by the following factors in descending order of importance (1) size of cavity 6 cm or more in diameter, (2) a history indicating onset more than 8 weeks before admission, (3) staphylococcic infection, and (4) location of abscess in lower lobe of either lung

Left Pulmonary Artery and Respiratory Obstruction —In case of aberrancy of the left pulmonary artery, this vessel arises in the right mediastinum and passes posteriorly between the trachea and esophagus to the left lung, resulting in obstruction of the trachea or right main-stem bronchus The authors summarize data on 15 patients with this anomaly, all but 2 of whom were young infants This anomaly is more common than is generally appreciated The diagnosis of aberrant left pulmonary artery should be considered in all infants with persistent stridor Physical findings may include stridor, retraction, tachypnea, wheezing, hyperresonance on the right with tracheal deviation to the left, and cyanosis The most common roentgenologic picture is that of emphysema of the right lung with mediastinal shift to the left A lateral view may show narrowing of the lower trachea The authors found combined tracheo-esophagraphy, utilizing the "gulp" technique, the most important diagnostic aid From 5 to 10 cc of an aqueous contrast medium is instilled into the posterior pharynx followed immediately by occlusion of the nose and mouth This causes the patient to swallow and aspirate, allowing simultaneous visualization of the esophagus and tracheobronchial tree The aberrant pulmonary artery is outlined by the resultant filling defects in the posterior trachea and anterior esophagus Surgical correction of this anomaly is achieved by dividing the aberrant pulmonary artery and re-anastomosing it in front of the trachea A right anterolateral approach gives the optimum exposure

Mitral Commissurotomy in Pregnancy —In the University Hospital, Turin, Italy, observations were made on 37 women subjected to mitral commissurotomy during pregnancy Nine had a history of rheumatic fever and 15 of repeated episodes of tonsillitis Peripheral emboli had occurred in 10 patients Twenty-two patients had had 1 to 4 pregnancies, 6 had had abortions, 11 were in their 1st pregnancy None of the women died during or after the commissurotomy The cardiocirculatory conditions showed great or satisfactory improvement in 32 of the 37 women, but in 5 slight exertional dyspnea and palpitation were still present, although the general condition had improved One of these patients had an associated aortic insufficiency and 4 had an associated mitral insufficiency before operation Thirty of the patients had a normal delivery, 1 had a successful cesarean section, in 3 women the pregnancy has not yet reached term, and in 3 the fetus died in utero after the maternal commissurotomy As regards the indications for mitral commissurotomy during pregnancy the authors say (1) A history of previous pregnancies without signs of cardiac or circulatory failure suggests that medical treatment can be tried (2) Progressive cardiovascular deterioration before or during gestation is an indication for prompt surgical treatment (3) The sudden onset of pulmonary edema indicates a downhill and is an indication for surgery (4) In combined valvular lesions every factor must be considered (5) Surgery should cure the established symptoms and prevent future manifestations, therefore commissurotomy should be performed in every case of pure mitral stenosis Mitral stenosis is not an indication for a therapeutic abortion

Journal Obst & Gynaec Brit Empire, London

67 177-352 (April) 1960 Partial Index

Basal Body Temperature Recordings in Gynecology and Obstetrics
F Benjamin p 177
Pregnancy After Vulvectomy for Carcinoma of Vulva
A A Gemmell and M Haines p 199
Brain Disease in Stillborn Infants and Neonates
P E Sylvester p 219
Incidence of Supine Hypotensive Syndrome in Pregnancy
F Holmes p 254
Study of Adeno acanthoma of Uterine Body
W Chanen p 287

Supine Hypotensive Syndrome in Late Pregnancy —Many observers have noted that there is a tendency for women in the late stages of pregnancy to experience a fall in blood pressure when supine To obtain information on the incidence and variation in intensity of this postural hypotension, 500 women, all pregnant for 36 or more weeks, were examined in the course of their routine antenatal visits, 180 were parous and 320 primigravidas The total number of antenatal studies was 616 Those women who had exhibited marked fall in blood pressure were examined again some days after delivery The subjects lay in the supine posture and blood pressure and pulse estimations were obtained at minute intervals for 6 minutes or longer Six grades of hypotension were differentiated Among the 148 women who experienced no fall in systolic pressure or only an insignificant one (grade 1), 45 exhibited a rise in diastolic pressure When the systolic pressure fell by more than 50% (grade 6) the pulse rate, after an initial rise, dropped precipitously, while a grade 4 or 5 fall was accompanied by tachycardia Hypotension of grades 3 to 4 was always attended by reduction in pulse pressure Signs of intolerance to the supine position were noted in connection with hypotension, namely restlessness, hyperpnea, pallor, desire to flex hips and knees, dizziness and faintness Some subjects refused to remain supine, others appeared to faint The likelihood of circulatory collapse occurring in a patient undergoing cesarean section under spinal analgesia exists whenever marked supine hypotension is elicited before operation Postural hypotension often became less marked as term approached and this change could be related to the descent of the fetal head into the pelvis

Adeno-acanthoma of the Uterine Body —From 1950 to 1957 inclusive there were 180 patients with cancer of the uterine body admitted to The Royal Women's Hospital, Melbourne, and in 42 the tumor was an adeno-acanthoma (24%) The pathological diagnosis of adeno-acanthoma was made from microscopic examination of endometrial scrapings or of the uterine contents after hysterectomy, the criterion for diagnosis being the presence of an adenocarcinomatous tumor containing islands of squamous epithelium The adenocarcinomatous component of the tumor was usually well differentiated, but high differentiation did not preclude the possibility of metastasis The degree of malignancy of adeno-acanthoma was at least comparable with that of ordinary endometrial carcinoma Extra-uterine metastasis occurred in 10 of the 42 patients The incidence of lymph node metastasis in patients subjected to radical surgery and lymphadenectomy (3 of 15 patients) suggests a place for this form of surgery in patients able to tolerate it Almost half the adeno-acanthomas treated with radiotherapy were radiosensitive In this series adeno-acanthoma of the uterine body was more frequent, more malignant, metastasized more readily, and was more radiosensitive than is generally believed

Lancet, London

1 835 886 (April 16) 1960 Partial Index

Tropical Eosinophilia
J K G Webb and others p 835
Nephrotic Syndrome
R G Mitchell p 843
Control of Poliomyelitis with Inactive Virus Vaccines
D S Dane and others p 845
Passage of Air Through Pharynx in Anesthetized Patients
H Ruben and others p 849
Venoarterial Shunts in Cirrhosis of the Liver
J Georg and K Mellemgaard p 852

Nephrotic Syndrome —Five children with the nephrotic syndrome who had not responded satisfactorily to 1 or more courses of hormone therapy were treated with large doses of cortisone given intermittently for long periods as advocated by Lange and co-workers (1953) All the children were girls ranging in age from 4½ to 12¾ years, and all had severe edema hypoalbuminemia and proteinuria which had lasted from 9 months to 3 years Treatment was started with a dosage of 20 mg of corticotropin given intramuscularly twice daily for 14 days It resulted in satisfactory diuresis and disappearance of edema in all but 1 patient, whose edema did not disappear completely until the 2nd week of maintenance therapy Five days after the course of corticotropin was completed, treatment with cortisone acetate was begun by giving 100 mg by mouth every 6 hours for 3 consecutive days, the total amount being 1200 mg After 4 days without hormone treatment this 3-day course was repeated for 20 weeks in the first 3 patients and for 52 weeks in the later treatment of all the patients One tablet of penicillin G (200,000 units) was given twice daily and is being continued in all except 1 patient This treatment enabled all the children to resume normal activities Three have been in complete remission for 12 to 30 months since treatment with cortisone was stopped, but 2 relapsed after maintenance treatment was withdrawn The results of treatment in this small series suggest that intermittent high-dosage steroid therapy is worthy of trial in every patient with the nephrotic syndrome who has not responded to standard hormone therapy Although cortisone is satisfactory, prednisolone in equivalent dosage would probably be preferable in the future

Control of Poliomyelitis —Low-titre neutralizing antibody developed in 8 of the 11 cynomologus monkeys which were given a single 10 ml dose of commercial (Salk) poliomyelitis vaccine Seven of these were protected when challenged 1 week later with a virulent strain of type 1 polio virus In the pathogenesis of poliomyelitis in cynomologus monkeys, throat virus seems to play an important part. It may be equally important in the dissemination of the disease in man Single large doses of inactivated vaccine might give useful protection in an epidemic

New England Journal of Medicine, Boston

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Prednisone and Aspirin in Rheumatic Heart Disease
A G Kuttner and others p 895
Drug Dosage for Patients of Varying Sizes
A M Butler and R H Richie p 903
Nevoid Syndrome
R J Gorlin and R W Goltz p 908
Low Leukocyte Alkaline Phosphatase
K R Tanaka and others p 912

Prednisone and Aspirin in Rheumatic Heart Disease —A combined rheumatic carditis study was organized between Jan 1, 1956 and Jan 1, 1959, in which the Children's Cardiac Services of hospitals in New York City, Baltimore, Boston and Cleveland participated Prednisone was given to 29 Children, and acetylsalicylic acid to 28 The patients ages ranged from 1 to 12 years Only patients who suffered rheumatic fever for the 1st time, who had clinical evidence of moderate to severe carditis, and in whom the onset of rheumatic manifestations had occurred within 28 days before treatment were included in this study The comparison of the effect obtained with a total dose of 3 Gm of prednisone given for a period of 12 weeks with that of a therapeutic dose of acetylsalicylic acid given for a similar length of time showed that the value of the two drugs was essentially the same The effect of both prednisone and acetylsalicylic acid appears to consist mainly in the supression of the inflammatory reaction caused by the disease In many patients, however, even when the acute symptoms were promptly and well controlled, cardiac damage could not be prevented

Revista brasileira de cirurgia, Rio de Janeiro

39 75-200 (Feb) 1960 Partial Index

Surgical Treatment of Tumors of Parotid
A L M Coutinho p 77
Prolonged Extracorporeal Circulation with Minimal Hemolysis
D J de Moraes and others p 129

Extracorporeal Circulation with Minimal Hemolysis —In spite of the advances concerning oxygenators and blood pumps, blood changes during heart surgery are the main cause of postoperative morbidity and mortality A procedure to minimize these limitations by diluting the blood during perfusion and using plasma instead of blood in the oxygenator was studied on 3 dogs weighing 12 to 16 kg (26-35 lbs) and subjected to perfusion for 120 minutes under hemodynamic and biochemical control A De Wall-Lillehei oxygenator was filled with 1,500 to 2,000 cc of plasma from blood collected in heparin 24 hours before the operation As soon as the perfusion was started the animals were put under by-pass with complete clamping of the venae cavae, they were kept thus for 2 hours At the end of perfusion protamine sulfate was administered in a dose twice as high as that of heparin, and 400 to 600 cc of erythrocyte mass was transfused The dogs survived and were observed for longer than 2 weeks without showing any signs of abnormality Hemolysis was only 20, 30, and 60 mg per 100 cc, respectively, in the 3 dogs The advantages of this procedure, as shown in the experimental study, are reduction in the number of blood elements traumatized avoidance of strange cells which are more sensitive to trauma, reduction in blood viscosity, and possible protection of cellular elements by the plasma The possibility of reducing blood trauma has especial meaning for treating complex cardiopathies such as tetralogy of Fallot and certain rheumatic valvular lesions

Revista clinica española, Madrid

76 145-212 (Feb 15) 1960 Partial Index

Cycloserine in Chronic Pulmonary Tuberculosis
F Tello and others p 159
Coronary Hemodynamics in Cardiac Arrhythmias
P Zarco D W Irving and E Cordas p 163
Gastroduodenal Ulcer New Theory and Therapy
C A Soler p 170

Gastroduodenal Ulcer —According to the hypothesis presented in this article, primary lesions of trophic infectious, or other origin cause atrophy of the Oppel's cells in Brunner's glands and perhaps also in Panet's cells of the Lieberkuhn's glands Consequently the pancreatic function is decreased and food is imperfectly digested As the insufficient pancreatic juice does not reach the stomach to inhibit the formation of gastric juice, more gastric juice is produced to stimulate the production of secretin Eventually hyperacidity produces lesions in the gastric mucosa The same mechanism explains the development of duodenal ulcers, and the vagal hypertonus in peptic ulcers is a consequence, not a cause of the lesions Based on this concept the author treated 112 patients with injections of secretin, administering daily injections for 10 consecutive days and following with a 10-day rest The usual alkaline and bismuth preparations were given at the beginning of therapy to patients with severe crises of acidity Of the 112 patients reported, 99 (88 4%) were clinically and radiologically cured, while 13 became asymptomatic but not radiologically cured Still better results were obtained when the secretin treatment was combined with administration of vitamin C

Revue de tuberculose et de pneumologie, Paris

24 213-436 (Feb -March) 1960 Partial Index

Pott's Disease Associated with Tuberculous Foci
P Jacob and others p 213
Tuberculosis of the Main Bronchi
J M Lemoine and J Denis p 258
Persistent Bronchial Fistulas
A Bernou and others p 283

Pott's Disease Associated with Tuberculous Foci—Between 1941 and 1956, 307 adult patients with Pott's disease associated with other tuberculous foci, especially pulmonary, were treated at the Centre Hospitalier Emile-Roux, Paris Those treated after 1947 received antibiotics (streptomycin PAS and INH), with pulmonary resection in exceptional cases With or without antibiotic therapy the patients with active Pott's disease were immobilized and a Berck's splint was applied, for those with high spinal lesions plaster splints were used Of 256 vertebral foci, 212 were treated with, and 44 without, posterior transplantation, 11 patients in the 1st group and 27 in the 2nd failed to obtain either cure or stabilization of the lesions Seventy-one patients died, of these, 13 died of non-tuberculous disease and 3 of post-operative complication Of the remaining 236 patients, 59 left the hospital before, and 177 after completing therapy One hundred twenty patients were followed up for different periods of time In 83, pulmonary and associated lesions were cured or stabilized, 13 had to be rehospitalized (1 with Pott's disease treated with bone transplantation), 24 died It is concluded that the main causes of aggravation of old lesions and localization of new ones, both before and after the advent of antibiotic therapy, were delayed diagnosis and irregular, incomplete, or delayed treatment Posterior vertebral osteosynthesis is still the treatment of choice provided the indications are precise and the technique adequate

Schweizerische medizinische Wochenschrift, Basel

90 333-356 (March 19) 1960 Partial Index

Differential Diagnosis of Diabetes Mellitus
G R Constam p 333
Osmotherapy for Elevated Intracranial Pressure
G Scharfetter and others p 342

Osmotherapy for Elevated Intracranial Pressure—One hundred patients with increased intracranial pressure due to space-occupying processes or cranial-cerebral trauma were admitted to clinic and were treated with intravenous infusions of an urea solution prepared by adding 70 cc of 10% invert sugar in water to each 30 Gm of urea crystals One or 1 5 Gm of urea was given per kilogram of body weight The infusion amount varied from 200 to 300 cc given at the rate of about 60 drops per minute In 10 patients the lumbar cerebrospinal fluid pressure was recorded continuously and simultaneously with the determination of the blood pressure and with electrocardiograms taken during and after the infusion of urea All of the patients showed a significant drop in cerebrospinal fluid pressure lasting for several hours, which occurred simultaneously with a slight increase in arterial blood pressure Similar but less marked results were obtained in 5 patients who were treated with intravenous infusions of mannitol Undesirable side effects were insignificant and consisted of headaches, occasional vomiting for a short period, and a feeling of dryness In addition to the rapid onset of the described urea effect (within 20 to 30 minutes after the institution of administration of the infusion), the absence of almost any associated risk, and the fact that the urea effect may be reproduced to an unlimited extent have been emphasized The mode of action of urea is an osmotic one Intracranial hemorrhage is a definite contraindication to osmotherapy Patients with severe renal or cardiac insufficiency should not be subjected to treatment with urea and mannitol

Scottish Medical Journal Glasgow

5 189-230 (May) 1960 Partial Index

Goiter and Cretinism Due to Abnormal Thyroid Compound
E M McGirr and others p 18
Control of Thyroid Secretion
I C Gilliland p 20

Goiter and Cretinism Due to Abnormal Thyroid Compoun
—Goitrous cretinism which is usually familial and genet has been shown by means of radioactive iodine (I^{131} studies to be due to various intrathyroid *enzyme* deficiencie The authors list 3 defects and suggest that in son cases of sporadic goitrous cretinism other intrathyro enzyme deficiencies remain to be defined They prese clinical, laboratory, and pathological findings in 6 patien who each suffered from an abnormal synthesis of thyro hormone of a type not previously clearly defined The ch metabolic manifestation of this was the formation of abnormal iodinated thyroid compound This compound a derivative of it, from which thyroxine was released wi difficulty, spilled over into the blood The result of th defect was difficulty in supplying enough thyroid hormo to the tissues The thyroid enlargement is presumed to a compensatory attempt to secure an adequate suppl hormone If the compensation is adequate the patient r mains euthyroid, if it is inadequate hypothyroidism is t presenting feature The clinical data show that goitro members of the same family may be either euthyroid hypothyroid The familial incidence suggests that the defe has a genetic basis and is to be added to the rapidly gro ing list of inborn errors of metabolism The pathology the thyroid gland in cases of dyshormonogenesis is distin tive and the essential features are the same whatever t basic defect, whether the production of an abnormal io nated compound or impaired peroxidase, or dehalogen activity Since in 1 patient with impaired dehalogen activity histological evidence of carcinoma developed, patien with dyshormonogenesis should be carefully followed u

WASHINGTON NEWS

Health Care Issue Confronts Senate
Drug Research Spending
"Folk Medicine" Ads Charged
Milk Contamination
Polio Rate
Drug Regulations

SENATE RETURNS HEALTH CARE ACTION DUE

The Senate reconvened after the convention recess with leaders of both parties placing a priority tag on legislation dealing with health care for the aged However, the Republicans and Democrats made it clear in their party platforms they favored different approaches to the problem

The Democrats came out for a Social Security program of the type advanced in the House by Rep Aime Forand (D, R I) The House earlier this year rejected this plan providing for compulsory higher Social Security taxes, and instead approved a voluntary program of federal-state assistance for those found to be in actual need of help in meeting their health care financing

The Republican party health platform in general met the principles of the House measure, though it appeared to be more in line with the Administration's specific program involving deductibles and giving the needy aged the choice of contributing to either a federal-state medical insurance plan or private insurance with the government paying some of the cost

The American Medical Association has endorsed the House-passed bill as the best way of securing aid for those who really need it

The health care issue was before the Senate Finance Committee when the lawmakers came back to work The Committee planned no further hearings on the matter, and was expected to vote during the week of August 8 Apparently, the choice was between the House-passed bill and a compromise Social Security plan proposed by committee member Sen Clinton Anderson (D, N M)

After the Committee votes, the issue then will come before the full Senate If the Senate approves a different measure from the House, a House-Senate Conference Committee would be appointed to try and resolve differences

PRIVATE DRUG RESEARCH SPENDING RISES

The prescription drug industry reported spending $197 million on research and development last year, a record sum and 16 per cent higher than in 1958

The 1959 outlays on drug research and development amounted to 7 8 per cent of drug manufacturers pharmaceutical sales of more than $2 5 billion

The spending was hailed as "a typically American example of the force of private enterprise at work for the betterment of humanity," by Dr Austin Smith, President of the Pharmaceutical Manufacturers Association (PMA)

Here are some major findings of the third annual survey of industry research activities carried out in cooperation with the National Institutes of Health

- Drug industry research spending in 1959 was $7 million more than the companies estimated that it would be a year ago
- Over $18 million of the total was spent outside of pharmaceutical house laboratories in the form of grants and contracts to medical schools, hospitals, research institutes, and other institutions
- An estimated 100,200 chemicals, compounds, and other substances were prepared, obtained, and biologically tested by the industry in its search for new and more specific medicinals in 1959
- Of these substances, 36,000 were in the field of cancer chemotherapy The second heaviest concentration was 28,200 substances pertaining to allergies and infectious diseases
- The 140 producer members of the PMA, responsible for more than 95 per cent of ethical drug production in the United States, estimated research and development spending of $214 million in 1960

"FOLK MEDICINE" PUBLISHERS CHARGED

The Federal Trade Commission charged publishers of the best-selling book 'Folk Medicine' with falsely claiming it contains cures for various ailments which defy conventional medical treatment

The publisher, Holt, Rinehart, and Winston, Inc, New York, was accused of "falsely advertising" the book, written by Dr D C Jarvis, a Vermont physician

The FTC said the recommendations in the book, mostly dietary, will not arrest, correct, or cure such conditions as the common cold, arthritis, kidney trouble, digestive disorders, high blood pressure, overweight and obesity, chronic fatigue, headaches including migraine, hay fever, asthma, dizziness, run down feelings, lack of energy, sinus infections, or lack of fertility, and that it is not an adequate, effective or reliable treatment

Among other things, the book recommended apple cider vinegar and honey

Dr Philip White, Secretary of the A M A's Council on Foods and Nutrition, said in an article in *Today's Health* that "there is nothing in honey or in vinegar which can support the claims made by the author of this book"

MOVE AGAINST MILK CONTAMINATION

The Federal Trade Commission ordered wider warning requirements in order to prevent contamination of milk by antibiotics and other drugs which might leave a residue in milk

The Commission dispatched letters to all known primary producers of drugs requiring them to include in their advertising of drugs to be used on dairy animals a conspicuous warning of how long the animals' milk must be withheld from human consumption after the drug is administered

Previously, when antibiotics such as penicillin were sold for treating dairy animals, the drug label alone carried the warning

People who drink milk containing drug residues may be allergic to the drug, or may become so sensitized that they would suffer a bad reaction should the drug be administered to them later Principal drug involved is penicillin, used for the prevention or treatment of mastitis in cows

POLIO CASES RISE

The number of new polio cases rose across the nation during the third week of July, but new paralytic cases decreased, the Public Health Service reported During the week ending July 23, 105 new cases were reported, of which 63 were paralytic This compared with 95 cases the previous week, with 69 paralytic

Totals for the year were 724 cases, of which 518 were paralytic This is the lowest cumulative total of any previous year except for the paralytic total in 1958 For the same week a year ago, 276 cases were reported, of which 178 were paralytic

The increase in the number of cases for the latest week was slight in comparison to the increase of 46 cases in the previous week's tally

The PHS said Rhode Island and Puerto Rico continued as major epidemic areas, with an outbreak in South Carolina still increasing A new concentration of cases was reported in a section of Chicago

FDA PROPOSES NEW REGULATIONS FOR DRUGS

The Food and Drug Administration has proposed stricter regulations designed to insure that physicians receive adequate information about prescription drugs

The new regulations also would keep new drugs off the market until the safety of their manufacturing process is assured by inspection

An FDA announcement described the proposed changes in labeling of prescription drugs as "sweeping"

"Virtually all prescription drug packages and printed matter distributed to physicians to promote sale of a drug would be required to bear complete information for professional use of the drug, including information about any hazards, side-effects or necessary precautions," the FDA said

"Heretofore such fully detailed information has not been required in labeling when it was available in scientific literature, or, in certain cases, was available to the physician upon request The only exception in the proposed regulations would apply to frequently used medicines that are commonly familiar to the doctor"

The proposed labeling changes also would require drugs for injection and for use in the eyes to bear a quantitative declaration of all inactive ingredients Labels of all prescription drugs would be required to include an "identifying lot or control number from which it is possible to determine the complete manufacturing history of the drug" Exemptions would be permitted where there is insufficient label space provided the information is given on other parts of the drug package All labeling bearing information for use of a drug would be required to have the date of its issuance

The FDA said the proposed labeling changes would correct any tendency on the part of some manufacturers to describe to physicians the merits of a drug without giving information regarding its hazards and the special precautions necessary for maximum safety and effectiveness

To insure a new drug's safety, the new regulations would require that it be kept off the market until the FDA, by a factory inspection, had confirmed the manufacturer's representations regarding the reliability of manufacturing methods, facilities and controls

Such an inspection would verify that the firm can insure the identity, strength, quality, and purity of the drug, the FDA said Occasional inspections have shown conditions in manufacturing plants which were contrary to representations made by the manufacturer in his request for safety clearance, according to the FDA

Commenting on the proposed regulations, George P Larrick, Commissioner of Food and Drugs, said

"The large number of new medications has made it increasingly difficult for doctors and pharmacists to keep adequately informed about them We are hopeful that the proposed regulations will improve the communication of vitally necessary information and bring about a general improvement in drug promotion practices At the same time, they should furnish a basis for more effective government control where necessary"

The proposed regulations were published in the July 22 Federal Register and interested persons were invited to submit written comments within 60 days The new regulations could be adopted any time thereafter, but the comments might result in some modifications of the original proposals

The FDA has been under fire in recent months from a Senate subcommittee headed by Sen Estes Kefauver (D, Tenn) During the subcommittee's investigation of the drug industry, the FDA was charged with laxness in policing the industry However, FDA officials said the proposed new regulations were not the result of pressure from Congress but had been in the works for some time

HOW WOULD YOU DEFINE *the ideal diuretic?*

The qualities to be sought in an ideal diuretic have been listed[1] as follows:

"(1) Sustained rather than abrupt violent action.

(2) Reduced capacity for electrolyte upheaval

(3) Convenience of administration; self-administration (oral, rectal, or subcutaneous)

(4) Decreased toxicity (systemic and local irritant action, especially of the gastrointestinal tract).

(5) Effectiveness where others are ineffectual or contraindicated.

(6) Applicability in cases with a history of allergic reaction to other diuretics."

It would be rash to term any drug ideal It is safe to say, however, that Aldactone very closely approximates these six requirements. Most importantly, Aldactone often relieves edema and ascites resistant or not optimally responsive to conventional diuretics By blocking the *action* of the potent salt-retaining hormone, aldosterone, Aldactone, used alone or in synergistic combination with other potent agents, establishes satisfactory diuresis in most edematous patients who have heretofore been considered beyond the help of medical management Aldactone offers a fundamentally new approach to the control of edema in such disorders as congestive heart failure, hepatic cirrhosis, the nephrotic syndrome and idiopathic edema.

ALDACTONE® is supplied as compression-coated yellow tablets of 100 mg
(brand of spironolactone)

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[1] Modell, W Am J Cardiol 3 139 (Feb) 1959

Research in the Service of Medicine G D SEARLE & CO.

MEETINGS

AMERICAN MEDICAL ASSOCIATION Dr F J L Blasingame, 535 North Dearborn St, Chicago 10, Executive Vice-President
1960 Clinical Meeting, Washington, D C, Nov 28-Dec 1
1961 Annual Meeting, New York City, June 26-30
1961 Clinical Meeting, Denver, Nov 27-30
1962 Annual Meeting, Chicago, June 11-15
1962 Clinical Meeting, Los Angeles, Nov 26-29
1963 Annual Meeting, Atlantic City

AMERICAN

1960

August

American Association of Blood Banks, Jack Tar Hotel, San Francisco Aug 21-26 For information write AABB Central Office, Suite 1619, 30 N Michigan, Chicago 2

American Congress of Physical Medicine and Rehabilitation, Mayflower Hotel Washington, D C, Aug 21-26 Mrs Dorothea C Augustin 30 N Michigan Ave, Chicago 2, Executive Secretary

American Hospital Association, Civic Auditorium, San Francisco, Aug 27-Sept 1 Mr Maurice J Norby, 840 N Lake Shore Dr, Chicago 11, Secretary

American Institute of Ultrasonics in Medicine Statler-Hilton Hotel, Washington, D C, Aug 20 Dr Dorothy M Stillwell Dept of Phys Med and Rehab, Univ of Colorado Med Center, Denver 20, Chairman

American Physiological Society, Stanford University Calif, Aug 22-26 Mr Ray G Daggs, 9650 Wisconsin Ave, Washington 14, D C Executive Secretary

American Society for Pharmacology and Experimental Therapeutics, University of Washington Seattle, Aug 21-25 Dr Karl H Beyer Merck Sharp & Dohme Research Laboratories, West Point Pa, Secretary

American Veterinary Medical Association Denver-Hilton Hotel, Denver, Aug 15-18 H E Kingman Jr, 600 S Michigan Avenue, Chicago 5 Executive Secretary

Biological Photographic Association, Inc, Utah Motor Lodge, Salt Lake City Utah, Aug 23-26 Miss Jane H Waters, Box 1668, Grand Central P O New York 17, Executive Secretary

Conference on the Chemical Organization of Cells Normal and Abnormal, University of Wisconsin, Madison, Aug 25-27 Dr J F A McManus, Dept of Pathology, University of Alabama Medical Center, Birmingham Chairman

Reno Surgical Society, Mapes Hotel, Reno, Nev, Aug 18-20 Dr Gilbert G Lenz 505 S Arlington Ave, Reno, Nevada

Rocky Mountain Radiological Society, Denver-Hilton Hotel, Denver Aug 11-13 Dr John H Freed, 4200 E 9th Ave, Denver 20, Secretary-Treasurer

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug 25-27 Mr Charles Lively, Box 1031, Charleston 24, W Va, Executive Secretary

September

American Academy of Pediatrics, and American Academy of General Practice, Louisiana Chapter, Roosevelt Hotel, New Orleans, Sept 23 Dr Herbert B Rothschild, 1520 Louisiana Ave, New Orleans 15, Chairman of Publicity Committee

American Association for Automotive Medicine, Dearborn Inn, Dearborn, Mich, Sept 19-20 For information write Dr H A Fenner Jr, 115 W Sanger St, Hobbs, N M

American Medical Writers' Association, Hotel Morrison, Chicago, Sept 30-Oct 1 Dr Harold Swanberg, 510 Maine St, Quincy, Ill, Secretary

American Roentgen Ray Society, Ambassador Hotel, Atlantic City, Sept 27-30 Mr Hugh Jones, 20 N Wacker Dr, Chicago 6, Director, Public Relations

American Society of Clinical Pathologists, Palmer House, Chicago, Sept 24-Oct 2 Mr Claude E Wells, 445 Lake Shore Drive, Chicago 11, Executive Secretary

College of American Pathologists, Palmer House, Chicago, Sept 24-27 Dr Arthur H Dearing, 2115 Prudential Plaza, Chicago, Executive Director

Colorado State Medical Society, Stanley Hotel, Estes Park, Sept 14-17 Mr Harvey T Sethman, 835 Republic Bldg, Denver 2, Executive Secretary

Delaware, Medical Society of, Rehoboth, Del, Sept Mr Lawrence C Morris Jr, 1925 Lovering Ave, Wilmington 6, Del, Executive Secretary

Flying Physicians Association, third clinical meeting, Western Hills Lodge, Wagoner, Okla, Sept 6-9 For information write Flying Physicians Association National Headquarters, P O Box 3275, Tulsa Okla

Inter-Society Cytology Council, Palmer House, Chicago, Sept 23-25 Dr Paul A Younge, 1101 Beacon St, Brookline 46, Mass, Secretary

Kentucky State Medical Association, Louisville, Sept 20-22 Mr J P Sanford, 1169 Eastern Parkway, Louisville 17, Ky, Executive Secretary

Maryland, Medical and Chirurgical Faculty of the State of, Semiannual Meeting Ocean City, Sept 16 Mr John Sargeant, 1211 Cathedral St, Baltimore 1, Executive Secretary

Michigan State Medical Society, Detroit, week of Sept 25 Dr D Bruce Wiley, 606 Townsend St, Lansing 15, Mich, Secretary

Montana Medical Association, Baxter Hotel, Bozeman, Sept 15-17 Dr William E Harris, 114 N Second, Livingston, Montana, Secretary

National Cancer Conference, American Cancer Society, Inc an the National Cancer Institute, Minneapolis, Minnesota, Sept 1 15 Dr Roald M Grant, 521 W 57th St, New York 19, Coordinat

National Recreation Congress, Shoreham Hotel, Washington D C, Sept 25-29 Willard B Stone, 8 W Eighth St, New York 11, Secreta

Nevada State Medical Association, Stardust Hotel Las Vegas Se 7-10 Mr Nelson B Neff, P O Box 2790, Reno, Nev, Execut Secretary

New England Society of Anesthesiologists, Bretton Woods N E Sept 18-19 Dr Thomas K Burnap, P O Box 81, Kenmore Sta P O, Boston 15

Oregon State Medical Society, Portland, Sept 7-9 Mr Roscoe K Miller, 2164 S W Park Place, Portland 5, Ore, Executive Secretary

Pacific Dermatologic Association, Empress Hotel, Victoria, Brit Columbia, Canada, Sept 1-4 Dr Edward J Ringrose 2636 Telegraph Ave, Berkeley 4, Calif, Secretary-Treasurer

Society for Pediatric Radiology, Ambassador Hotel Atlantic City N J, Sept 26 Dr Richard G Lester, 412 Union St S E Minneapolis 14, Minn,, Secretary-Treasurer

Southern Trudeau Society (and Southern Tuberculosis Conference), Hotel Francis Marion, Charleston, S C, Sept. 14 16 W Judson M Allred Jr, P O Box 9865, Northside Station Jackson, Miss Secretary-Treasurer

Tennessee Valley Medical Assembly, Read House, Chattanooga Tenn, Sept 26-27 Dr Robert A Waters, 109 Medical Arts Bldg Chattanooga, Chairman

Tri-State Medical Assembly, Confederate Memorial Medical Center Shreveport, La, Sept 14 Dr J W Wilson Jr 940 Margaret Place Shreveport, La, Secretary-Treasurer

Utah State Medical Association, Hotel Utah Motor Lodge Salt Lake City, Sept. 20-23 Mr Harold Bowman, 42 S 5th East Salt Lake City 2 Executive Secretary

Washington State Medical Association, Seattle, Sept 25 28 Mr Ralph W Neill, 1309 Seventh Ave, Seattle 1, Executive Secretary

Wyoming State Medical Society, Jackson Lake Lodge, Moran Sept 7-10 Mr Arthur R Abbey, P O Box 2036, Cheyenne, Wyo, Executive Secretary

October

Academy of Psychosomatic Medicine, Benjamin Franklin Hotel Philadelphia, Oct 13-15 For information write Dr Bertram B Moss, 55 E Washington, Chicago 2

American Academy for Cerebral Palsy, Penn-Sheraton Hotel Pittsburgh, Oct 5-8 Dr Joseph D Russ, 1520 Louisiana Ave, New Orleans 15, Executive Secretary

American Academy of Ophthalmology & Otolaryngology, Palmer House, Chicago, Oct 9-14 Dr William L Benedict, 15 Second St S W Rochester, Minn Executive Secretary

American Academy of Pediatrics, Palmer House, Chicago, Oct 17 20 Dr E H Christopherson, 1801 Hinman Ave, Evanston, Ill, Executive Director

American Association of Medical Clinics, New Orleans Oct 6 8 Dr Joseph B Davis, 134 N Washington St, Marion, Ind, Secretary

American Association of Medical Record Librarians Olympia Hotel Seattle, Oct 10-13 Miss Doris Gleason, 840 N Lake Shore Dr, Chicag 11, Executive Director

American Association of Poison Control Centers, Palmer House Chicago, Oct. 18 Dr Harry C Shirkey, 712 S 30th St, Birmingham Ala, Chairman, Program Committee

American Association for the Surgery of Trauma, Coronado Hotel Coronado, Calif, Oct 5-7 Dr William T Fitts Jr, 3400 Spruce St Philadelphia 4, Secretary

American College of Gastroenterology, Bellevue-Stratford Hotel Philadelphia, Oct 23-26 Mr Daniel Weiss, 33 W 60th St, New Yor 23, Executive Director

American College of Surgeons, Clinical Congress, San Francisco Oct 10-14 For information write Dr William E Adams, 40 E Er St, Chicago 11

American Fracture Association, El Presidentia Hotel, Mexico, D F Mexico, Oct 30-Nov 4 Dr H W Wellmerling, 610 Griesheim Bldg Bloomington, Ill, Executive Secretary

American Heart Association, Inc, Jefferson Hotel, St Louis, Oct. 2 25 Mr Rome A Betts, 44 E 23rd St, New York 10, Executive Directo

American Otorhinologic Society for Plastic Surgery, Inc, Conr Hilton, Chicago, Oct 9 Dr Joseph G Gilbert, 75 Barberry Lane, Rosly Heights, L I, New York, Secretary

American Public Health Association, San Francisco Oct 30 Nov Dr Berwyn F Mattison, 1790 Broadway, New York 19, Execut Director

American Rhinologic Society, Belmont Hotel, Chicago, Oct 8 D Robert M Hansen, 1735 N Wheeler Ave, Portland 17, Ore, Secreta

American School Health Association, San Francisco, Oct 30 Nov Dr A O DeWeese, 515 E Main St., Kent, Ohio, Executive Secreta

American Society of Anesthesiologists, Inc, Statler Hilton, N York City, Oct 2-7 Mr John W Andes, 515 Busse Hwy, Park Rid Ill, Executive Secretary

American Society of Facial Plastic Surgery, Chicago Oct 13 I Samuel M Bloom, 123 E 83d St, New York 28, Secretary

American Society of Plastic and Reconstructive Surgery, Stat Hotel, Los Angeles, Oct. 2-7 Dr Thomas R Broadbent, 508 E Temple, Salt Lake City, Secretary

Association of American Medical Colleges, Diplomat Hotel, Hollywood Beach, Fla, Oct 31-Nov 2 Dr Ward Darley, 2530 Ridge Av Evanston, Ill, Executive Director

Association of Life Insurance Medical Directors of America, Statle Hilton Hotel, New York City, Oct. 19-21 Dr Royal S Schaaf As Med. Dir, Prudential Insurance Co of America, Newark, N J, Secreta

Association of Medical Illustrators, La Salle Hotel, Chicago, O 3-5 Miss Rose M Reynolds Univ of Nebraska Coll of Med., 42 Dewey Ave, Omaha 5, Recording Secretary

(Continued on page 42)

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CURRENT THERAPY OF SYSTEMIC LUPUS ERYTHEMATOSUS

A COMPARATIVE EVALUATION OF CORTICOSTEROIDS AND THEIR SIDE EFFECTS WITH EMPHASIS ON FIFTY PATIENTS TREATED WITH DEXAMETHASONE

Edmund L Dubois, M D , Los Angeles

The current clinical concept of systemic lupus erythematosus is reviewed on the basis of a 10 year study of 400 patients treated with rest, salicylates, antimalarials, and corticosteroids Particular attention was given to the therapeutic value and side effects of the corticosteroids Fifty patients received dexamethasone for periods up to 15 months The maximum dose was 24 mg per day for three weeks and the average maintenance dose was 2 7 mg per day Clinical improvement closely paralleled that obtained by other corticoids Side effects included edema (28 %), hirsutism (28 %), and insomnia (8 %), and serial upper gastrointestinal roentgenograms performed in 28 patients revealed peptic ulcers in 5 There was a disappearance of all the clinical and laboratory abnormalities produced by the disease with the exception of longstanding renal involvement

SYSTEMIC lupus erythematosus (S L E) is a malignant variant of rheumatoid arthritis, with one case of S L E being seen at our hospital for every 14 of the latter During the past 10 years, 400 patients with various forms of S L E have been treated under my supervision, with rest, salicylates, antimalarials, and corticosteroids The aim of this report is to review the current status of therapy with emphasis on relative differences in both therapeutic and side-effects of the older anti-inflammatory hormones compared to dexamethasone (9 alpha-fluoro, 16 alpha-methylprednisolone) Particular attention has been paid to the incidence of peptic ulceration induced by corticosteroids Ninety-four patients have received a total of 301 gastrointestinal x-rays in order to evaluate this aspect of the problem

Description of the Disease

Systemic lupus erythematosus is usually a chronic, recurrent multisystemic disorder similar in clinical picture and course to rheumatic fever and rheumatoid arthritis The fulminant form of the disease, with death in a matter of weeks, has been seen but once in my experience with 400 cases The occurrence of systemic lupus erythematosis at the 3,500 bed Los Angeles County General Hospital is almost as frequent as any of the following diseases leukemia, acute rheumatic fever, serum sickness, and pernicious anemia

The clinical characteristic which suggests S L E rather than one of the other 'connective tissue' disorders is the appearance of involvement in many systems Eighty-eight per cent of the patients are female The age of onset in most patients is from 10 to 40 years, with a median of 25 years The disease is characteristically subject to many remissions and exacerbations In one detailed study of this feature, spontaneous improvement occurred at least once prior to steroid therapy in 38 7% of 163

From the Department of Internal Medicine The University of Southern California School of Medicine and the Los Angeles County General Hospital patients [1] The problem of diagnosis in this ailment is rendered more difficult by its protean manifestations and by the fact that there is no classic pattern of the disease Any system may initially be affected and heal months or years later the same or another area may become involved It is only by performing a thorough history and physical examination that the full picture of the natural evolution of this ailment can be obtained and the diagnosis suggested

In one series of 62 patients, 34% initially developed a rheumatoid-like arthritis, however by the time the diagnosis was made, at least 90% had had similar symptoms, many of whom had rheumatoid nodules [2] Often the early arthritis is primarily a periarticular inflammation or may be a mere arthralgia or morning stiffness, without overt joint changes Later, joint effusion and classic rheumatoid deformities may occur Cutaneous eruptions of various types across the cheeks and bridge of the nose were presenting symptoms in 16 1% of the patients These lesions vary from typical classic scaly erythematous eruptions of systemic lupus to small atypical discoid lupus-like plaques Cutaneous eruptions, as initial symptoms appeared elsewhere on the body in 11 3% of patients These lesions varied in appearance from hives to maculae and bullae Other presenting manifestations included such diverse entities as Raynaud's phenomenon, hemolytic anemia, pleurisy with and without effusion, false-positive serologic tests for syphilis, pericarditis, fever, cachexia, renal disease usually of the nephrotic type, and epilepsy

If a patient has had one or more of the changes enumerated above, such as rheumatoid-like arthritis with skin lesions of discoid lupus or arthralgia with a hemolytic anemia, the diagnosis of S L E should be considered and the L E cell test performed In approximately 80% of typical clinical cases the illness can be confirmed after repeated testing over a period of months by finding L E cells which are probably pathognomonic of the disease If cutaneous lesions are present, skin biopsy may confirm the diagnosis in another 10%, while diagnosis in the final 10% often depends upon clinical data alone Confirmation of the diagnosis in this latter group is often obtained postmortem Numerous other tests have been devised for this purpose, such as various complement-fixation procedures, precipitin tests, agglutination reactions, and fluorescent antiglobulin studies, none of which are as specific as the L E cell preparation The paratoluenesulfonic acid precipitation test which has recently been advocated as a simple specific test is so nonspecific as to be positive in apparently all diseases which produce hyperglobulinemia [3]

L E cells can be found in about 5% of patients who apparenty have rheumatoid arthritis without multisystem involvement at the time of the test The positivity of the test in this group is just as great as in classic S L E, contrary to the stated diagnostic criteria employed by the American Rheumatism Association [4] Prolonged observation of these patients will be necessary to determine whether most of them will terminate in classic overt systemic lupus erythematosus confirmed at autopsy

Principles of Therapy

Treatment depends upon the clinical severity of the illness If the presenting problem is a false positive serologic test for syphilis in an asymptomatic patient who has a few L E cells, no specific therapy is necessary The patient should be reassured of the usually benign course of this form of the disease and closely observed If the main complaint is mild rheumatoid arthritis or a rheumatic fever-like picture, this often can be adequately controlled by modified bed rest and administration of salicylates, which should be increased in amount to the point of salicylism The frequent use of these drugs should be encouraged since they reduce the requirements for antimalarial and steroid therapy None of my patients have ever been allergic to salicylates An increased amount of bed rest is usually helpful in controlling symptoms in the active stages of the disease, in addition to other treatment If salicylates and rest fail, or if cutaneous lesions are present, antimalarial therapy should be instituted The preferred drug at present is hydroxychloroquine (Plaquenil) in a dose of 200 mg, three or four times daily, since no serious side-effects have been reported from its use Chloroquine (Aralen) phosphate 250 mg, twice daily can be used In a rare patient who has received it over a period of many months or longer, corneal deposition may occur [5] This is usually gradually reversible when the medication is stopped There is no good evidence that retinopathy can be produced by this substance [6] Retinal vascular disease and degeneration have been reported in systemic lupus prior to the advent of antimalarial therapy [7] Amodiaquin (Camoquin) 200 mg, twice daily, is also a relatively safe agent Atabrine (100 mg twice daily) is now only rarely used by me because of the occurrence of aplastic anemia in one of my patients on long-term therapy and its appearance in about 1 in 25,000 patient years of exposure for military personnel on atabrine antimalarial prophylaxis [8] Nausea, anorexia, vomiting, and diarrhea occur not infrequently with one or the other of these chemicals and this necessitates occasional changes in drug or dosage schedules Seven to sixteen per cent of patients develop a dermatitis from one antimalarial drug and will usually not have a recurrence when transferred to another Details of antimalarial therapy have been published elsewhere [1] If salicylates and antimalarials fail to control the disease or if the patient is critically ill, or has neurological or renal involvement, steroid therapy should be started

The dosage of corticosteroid required varies directly with the severity of the disease In the milder cases the estimated amount of hormone is merely added to the therapeutic regimen of the patient Often this means supplementing a combination of salicylates and antimalarials with small doses of steroids Periods of a week or more are permitted to lapse between dosage changes in the milder cases The increments used here are small, perhaps a 10 to 20% rise at intervals until symptomatic and laboratory improvement is noted Similar decrements are utilized in withdrawing steroid therapy No corticotropin is employed Often, larger than expected amounts of the newer synthetic unsaturated steroids (prednisone, prednisolone, triamcinolone, methylprednisolone, and dexamethasone) must be used to control exacerbations of the disease since these hormones are not as predictable in their effects as are the older corticosteroids, such as cortisone and hydrocortisone Whenever more than 50 mg per day of cortisone or its equivalent in other steroids is used for longer than a few weeks a prophylactic ulcer regimen should be instituted consisting of six feedings, antacids, and anticholinergic therapy

Treatment of the Severely Ill Patient

In the severely ill patient, salicylates and antimalarials are not given early in therapy but the patient is immediately given large doses of steroids, such as 400 mg per day of cortisone This is done initially so as to rapidly reverse the pathological process before irreversible damage is done If no response occurs within 24 to 48 hours then the dosage of steroid is increased by 25 to 100%, depending on the situation, until improvement is noted As much as 4,000 mg per day of cortisone or its equivalent in other steroids has been used successfully in treating acute L E crises It is advisable to continue using high dosages of steroids until all acute abnormal physical findings have subsided Early renal involvement is usually benefited by large doses of these hormones The clinical characteristics are the absence of hypertension, occasional azotemia, presence of proteinuria, hematuria, and casts of the red cell, granular, and hyaline type A nephrotic syndrome is often an early manifestation, which may also be benefited If after two months of steroid treatment improvement has not occurred, nitrogen mustard is often helpful Advanced nephropathy with hypertension and anasarca is usually aggravated by large amounts of corticoids since oliguria, grand mal seizures, and death often rapidly ensue after their administration Nitrogen mustard is occasionally helpful in this terminal stage Chlorothiazide and hydrochlorothiazide are useful in controlling the edema associated with nephropathy Many patients develop cutaneous reactions from one of these diuretics, but the lesions do not necessarily recur on changing to the other Mercurials should be used with caution since severe anaphylactic reactions are more likely in patients with S L E than others

The clinical picture and hemoglobin level are used as the major guides to steroid therapy If significant renal involvement is present, this is closely followed in order to determine when to reduce the dosage The sedimentation rate is never used as the main index to dosage, since it can remain indefinitely elevated in some patients, despite complete clinical remissions The L E cell test is helpful in following the over-all picture of the disease, but should not be used as a basis to determine therapy because it requires several weeks for changes to occur Many patients have persistently positive L E cell tests even though they are in a remission requiring no medication

Salicylates and antimalarials have a synergistic anti-inflammatory effect and are often used together when tapering the dose of steroid once a remission has been induced in a critically ill patient

Dexamethasone Therapy

Clinical Material—Fifty patients with active systemic lupus erythematosus received dexamethasone for periods of 1 to 15 months The diagnosis was confirmed by the finding of L E cells in 37 (74%), positive skin biopsies, with negative L E cell tests in 8 (16%), and in 5 patients (10%) by clinical picture alone Only one of the patients merely had rheumatoid arthritis with L E cells and no multisystem disease There were 46 females (92%) and 4 males (8%) This series is comparable to similar groups reported by me and treated with corticotropin and cortisone, prednisone and prednisolone, triamcinolone, and methylprednisolone [9] Many of these patients have received most of these steroids at some time during their course (see addendum)

Twenty-four patients were receiving salicylate therapy to the point of mild toxicity with their steroids, and 17 were concurrently taking antimalarials Ulcer diets and anticholinergic therapy were given to three patients with a history of peptic ulcer and to none of the others unless a dexamethasone-induced ulcer appeared Six patients initially were on a sodium restricted diet when administration of the new steroid was instituted Supplementary potassium therapy was not used unless clinical or chemical evidence of hypopotassemia appeared

Dosage of Dexamethasone—In 29 patients, steroid therapy was initiated with dexamethasone in a dosage ranging from the addition of 1 0 mg per day, to the therapeutic regimen of patients who were on salicylates and antimalarial therapy, to 6 0 mg in a woman seriously ill with a severe hemolytic anemia This patient's illness was not adequately controlled until the dose was increased to 20 mg per day In the other 21 cases the disease had stabilized on therapy with other steroids and the patients were then transferred to dexamethasone The new steroid was usually given in two divided doses daily except in the occasional patient who noted arthralgia between the 12-hour medication periods, in which instance the dose was divided into three or four parts The total period of observation was 266 patient months

Nine patients whose illness had stabilized on methylprednisolone (Medrol) therapy were changed to dexamethasone The new steroid was 8 0 times more potent than methylprednisolone, a dexamethasone ratio of 8 0 This was determined by dividing the dose of methylprednisolone needed for maintenance by the dose of dexamethasone required for identical clinical effects The range of dexamethasone varied from 5 3 to 13 3 times as potent To ascertain the amount of dexamethasone required to change a patient from methylprednisolone therapy to treatment with the new steroid, divide the therapeutic ratio into 1 For example, the ratio is 8 0 and the factor is ⅛=0 12 or 12% of the dose of methylprednisolone

Seven patients were transferred from hydrocortisone to dexamethasone therapy The median ratio in this group was 20 5 and mean 24 0 Three cases were changed from triamcinolone to the newer corticosteroid with a median ratio of 4 0 and a mean of 4 2 One patient each was transferred from cortisone with a ratio of 40 and another from prednisone with a ratio of 5

The maximum maintenance dose was 24 0 mg per day for periods of two and three weeks in two patients who were critically ill One of them had received gradually increasing doses of dexamethasone up to 18 mg per day for control of her active S L E After a protracted sun exposure she returned to the hospital with a generalized flare-up of her disease, with hematemesis Dexamethasone was increased to 24 mg per day parenterally but two weeks later hematemesis recurred and therapy was changed to parenterally administered hydrocortisone, 400 mg per day Three upper gastrointestinal series failed to disclose an ulcer The other patient had a severe peripheral neuritis and an agitated depressive reaction due to S L E For a month the dosage of dexamethasone was gradually raised from 1 to 16 mg per day, with little benefit Three weeks after elevating the steroid dosage to 24 mg per day the mental state, peripheral neuritis, and hemoglobin level showed marked improvement

Gastrointestinal Studies

Twenty-seven patients had a total of 58 upper gastrointestinal series performed to evaluate the ulcerogenic effects of this new steroid Fourteen had baseline studies immediately prior to institution of dexamethasone therapy and every few months during therapy The other 13 patients had examinations performed at several-month intervals while receiving this hormone Six new peptic ulcers were induced by the use of doses varying from 1 0 to 20 0 mg per day for periods of as short as two months to as long as 18 months of steroid therapy All the ulcers were symptomatic A total of 11 patients who received dexamethasone had epigastric distress and had routine x-rays throughout their course of therapy Five of these had demonstrable peptic ulcers Four were located in the antrum of the stomach and one in the duodenum An additional patient had repeated hematemesis and three normal x-ray studies Her symptoms disappeared after institution of a vigorous ulcer regimen and a change to parenterally administered hydrocortisone The location of the ulcers induced by corticosteroids is characteristically in the antral area Demonstrable lesions are found in the gastrointestinal tract of one half of the patients with ulcer symptoms, provided that frequent x-ray studies are performed There is no difference, in this respect, between the predni steroids, methylprednisolone, triamcinolone, and dexamethasone This has been demonstrated by a serial roentgenographic gastrointestinal survey of 94 patients receiving various doses of these steroids over periods up to three years The x-ray demonstrable incidence of peptic ulceration is also not significantly different between these various steroids varying from 18 to 22% There is a definite correlation between the incidence of ulceration and the dose of steroid employed Four of the six ulcers of patients on dexamethasone therapy appeared with doses of 2 25 mg per day or more of this steroid This correlates well with our findings of no ulcers in patients receiving 10 mg per day or less of prednisone or its equivalent in other steroids, 13% in those receiving 10 to 19 mg per day and rising up to 47% in patients taking over 60 mg per day for periods of several months[16]

Results of Therapy

The pattern of clinical improvement in systemic lupus erythematosus closely paralleled that obtained by previous treatment with corticotropin and other antiinflammatory hormones The fever abated within 24 hours, provided that the dose of corticosteroid was adequate Joint pains were greatly improved within several days Pleural effusion and cutaneous lesions subsided in one to several weeks Four patients had mild nephropathy of short duration characterized by normotension, albuminuria of about 2+, minimal edema, granular and hyaline casts and red cells, hypoalbuminemia without hyperchloresterolemia, and no or mild azotemia This completely cleared in all patients on dexamethasone therapy Nine patients had more advanced renal disease a nephrotic picture of anasarca, elevated cholesterol levels, nitrogen retention, and urinary sediments containing fatty casts and oval fat bodies All were treated with a low sodium diet as well as varying doses of dexametha sone. Only one was benefited by dexamethasone treatment. This is the 31-year-old patient, described in a previous communication, who obtained remissions of her nephropathy with prednisone and triamcinolone treatment.[9c] She developed severe proximal muscle weakness from the latter steroid which did not recur with administration of dexamethasone. Two of the patients who showed no improvement with dexamethasone therapy received nitrogen mustard, and one had an excellent result, while the other had only moderate benefit. Another patient in this group died of uremia. The other five are being maintained on steroid treatment for the present. Six of the patients in the group with advanced nephropathy received either chlorothiazide (Diuril) up to 2.0 Gm. daily, or hydrochlorothiazide (Hydrodiuril) up to 150 mg. per day, with temporary improvement in their edema in five.

Weight increase was a major problem in 64% of the patients. In only 2 patients (4%) did weight decrease, compared to 28% of a similar group of 40 cases treated with methylprednisolone and 18 (62%) of 29 patients treated with triamcinolone. Weight increased in 32 patients (64%) of the dexamethasone-treated group with a median change of 11 lb. (5.0 kg.). In 14 cases (28%) this was partially due to the accumulation of edema. Two of these patients subsequently developed acute pulmonary edema. Only three of these patients had a concomitant rise in blood pressure, which is characteristic of the other steroids. Generally the weight gain was associated with a greatly increased appetite and food intake (see addendum). Anorexia, which was a common problem in patients receiving triamcinolone, was not noted with this steroid. The weight changes which occurred were gradual and appeared over weeks or months. There was no weight change in 12 patients (24%) compared to 55% of the methylprednisolone-treated group and 28% of the triamcinolone-treated series.

The mean blood pressure was unchanged in 88% of this group compared to 68% of the methylprednisolone-treated series and 68% of the triamcinolone treated patients. It increased in 19% and decreased in 2%. Five patients showed a median rise of 20 mm. Hg, and one showed a decrease of 10 mm. Hg.

One patient had avascular necrosis of both femoral heads associated with systemic lupus erythematosus. There was only minimal improvement with use of as much as 8 mg. per day of dexamethasone. This complication of the disease has been seen in patients in our series of S. L. E., both in steroid-treated and untreated patients. Hormone therapy occasionally helps to relieve symptoms, but the x-ray findings do not change.[11]

Laboratory Changes

The hemoglobin level remained unchanged in one half of the cases. These patients had normal levels to start with since in most of them adequate control had been achieved with other steroids prior to transfer. The hemoglobin level increased a median of 1.9 Gm. in 10 cases (20%), compared to improvement in 38% of comparable series treated with methylprednisolone, and 35% with triamcinolone (see addendum).

White blood cell counts were unchanged in 50%. Twenty-eight per cent had a median rise of 3,000 per cubic millimeter, compared to 50% of the methylprednisolone-treated group and 34% of the triamcinolone-treated series.

The Wintrobe sedimentation rate (uncorrected at 60 min.) was unchanged in 52%, decreased in 14%, and increased in 8%. Inadequate data were available in 26%.

L. E. cell tests performed by the rotary method showed no change in quantity in 11 cases, full disappearance in 5, decrease in number in 1, increase in cells in two and remained absent in 26 cases.[12] There were inadequate data in five cases. The results are similar to those obtained with methylprednisolone and triamcinolone.

Originally 37 of these dexamethasone-treated cases had had L. E. cells at one time during the course of their illness. Adequate repeated L. E. studies are available in 34 of these cases. It is noteworthy that the cells disappeared in 20 of these, or close to 60% of this group, after one or more months of steroid treatment. In many of these cases the L. E. cells were no longer found prior to dexamethasone therapy.

Side Effects

The side-effects are reviewed in the table and results compared to other similar groups treated by the author with methylprednisolone, triamcinolone, and the prednisteroids.[13] Moon-faced appearance occurred in 60% of the dexamethasone-treated group, compared to 52% of the methylprednisolone-treated group, 45% of the triamcinolone-treated series, and 49% of the prednisteroid-treated cases. Fifty per cent of the patients who received dexamethasone as the initial steroid also became cushingoid. There was no significant difference in the incidence of this side-effect between the steroids nor was there a decrease in this alteration when the patient was transferred from one corticosteroid to another, provided a comparable dose was used. Once induced, this change persisted with administration of as little as 0.5 mg. of dexamethasone per day. As usual, this side-effect was less pronounced in the males. Three weeks to several months or more were required for development of this change.

Hirsutism occurred in 28% compared to 8% on methylprednisolone, 21% on triamcinolone, and 3% on prednisteroids. Acne appeared in 10% of both the new steroid and methylprednisolone series, compared to 17% of the triamcinolone-treated and 16% of the prednisteroid-treated groups. Striae formation was noted in 4% of this dexamethasone-treated group, compared to a high incidence of 14% in the triamcinolone-treated series

Ecchymoses were a problem with dexamethasone as they had been with methylprednisolone, occurring in 20% of the former group and 27% of the latter, compared to a 14% incidence with triamcinolone and 3% with prednisteroids These may appear with administration of as little as 1 0 mg per day of dexamethasone

Side-effects of Dexamethasone Compared to Those of Methylprednisolone, Triamcinolone, Prednisone, and Prednisolone

	Dexamethasone (50 Cases) %	Methylprednisolone (40 Cases)[9a] %	Triamcinolone (29 Cases)[9c] %	Prednisone and Prednisolone (37 Cases)[9b] %
Moon face, buffalo hump (cushingoid appearance) after transfer from older steroids				
Increased	10	5	14	12
Decreased	—0	3	0	5
Unchanged	10	22	14	17
Initial appearance as first steroid*	28	15	14	15
Initial appearance after transfer from other steroids†	12	8	3	0
None at any time	40	48	55	51
Total with cushingoid appearance	60	52	45	49
Marked hirsutism	28	8	21	3
Acne	10	10	17	16
Striae (marked)	4	3	14	3
Ecchymoses (marked)	20	27	14	3
Edema	28	5	3	6
Diabetes mellitus‡	4	0	3	6
Epigastric distress[10]	30	17	37	33
Muscle weakness	0	0	19	0
Insomnia	8	0	0	0
Psychosis	2	0	0	0

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* Twenty nine cases received dexamethasone as initial steroid, 14, or 28%, became "cushingoid "

† Twenty one cases were transferred to dexamethasone after receiving other steroids and 6 of these, or 28%, of this group became cushingoid

‡ Fasting blood sugar levels obtained in 15 cases before dexamethasone treatment and while on the maximum dose In one case the sugar rose from 77 to 147 mg % and in another from 97 to 239 mg %

The most disturbing side-effect of dexamethasone was the accumulation of pitting edema which appeared in 28% of this group, compared to 5% of the methylprednisolone-treated series, 3% of the triamcinolone-treated group and 6% of the prednisteroid-treated cases This change was noted in 11 patients without renal involvement Serum sodium levels were normal, but congestive heart failure appeared on two occasions, in a 50-year-old man with S L E , bronchial asthma, and cor pulmonale despite maintenance digitalis and chlorothiazide therapy, and in one 42-year-old woman with mild nephropathy, while on a low sodium diet (see addendum)

Fasting blood sugar values were obtained in 15 cases, before dexamethasone treatment and while on the maximum dose In only two instances did they definitely become elevated The data are not adequate to determine whether this new steroid induces less gluconeogenesis than the older ones

Epigastric distress immediately after intake of the medication was not noted Fifteen patients, or 30%, of the group complained of postprandial epigastric burning, eructation, and other symptoms of peptic ulceration The incidence of peptic ulceration has already been discussed Similar symptoms were present in 17% of the methylprednisolone-treated series, 37% of the triamcinolone-treated series and 33% of the prednisteroid-treated group[10]

Muscle weakness of the type described with triamcinolone therapy was not noted in any patient[9c] There were three patients who had developed weakness on triamcinolone, recovered fully on other steroids, and were subsequently treated with dexamethasone without recurrence Insomnia was a problem in four patients, and could be corrected by taking the hormone before supper or earlier during the day This had not been noted to be a significant problem in the use of the other steroids except with very large doses A psychosis characterized by severe depression and a feeling of unreality was induced by dexamethasone in one patient Upon withdrawal of the steroid it cleared and reappeared when she later was given hydrocortisone

Serial electrolyte studies were done in eight cases and whenever symptoms appeared in the others A low serum potassium level was the only abnormality noted in one instance in which the patient was also receiving chlorothiazide

Comment

Dexamethasone is an effective new unsaturated corticosteroid Its common side-effects are similar to those produced by older anti-inflammatory hormones except for the increased incidence of edema, epigastric distress, hirsutism, and insomnia There was no significant reduction in the occurrence of peptic ulcers induced by the new hormone

Of 21 patients who received prior steroid therapy, none were helped more by this new steroid than by the older ones (see addendum) Improvement in control without an increase in side-effects had been noted in 2 of 18 patients changed from other steroids to methylprednisolone and in 7 of 14 cases similarly transferred to triamcinolone This individual variability in response to the corticosteroids suggests that if the illness is inadequately controlled by increasing doses of one steroid, occasionally transfer to another may help As far as changing steroids to eliminate undesirable side-effects is concerned, the only ones I have seen disappear (provided the effective hormonal does in similar) are muscle weakness and excessive striae formation induced by triamcinolone The usual moon-face appearance is not benefited by hormone transfer The only effective means of combating all the side-effects is by reduction of the dose of steroid with synergistic therapy, including salicylates and antimalarials

Although the required dosage of dexamethasone is much smaller than that of the other corticosteroids in terms of milligrams, the side-effects are similar and the therapeutic benefit is no greater In fact, the hematological improvement produced by this newer hormone was not as good as that observed with the other steroids In addition, there is a great deal of variability in response The dose ranges between 12 to 40 times as powerful as hydrocortisone This great variability in dosage and individual unpredictability of action is common to all the synthetic unsaturated steroids from prednisolone to the newer ones, and consequently I prefer to initiate treatment in the average case of systemic lupus erythematosus with hydrocortisone, unless there is a problem of cardiorenal disease

Summary

Systemic lupus erythematosis (S L E) is a malignant variant of rheumatoid arthritis which occurs with one-fourteenth the frequency of the latter disease The overall incidence is almost as common as any of the following disease entities leukemia (all types), acute rheumatic fever, serum sickness, and pernicious anemia The diagnosis is confirmed by finding L E cells in 80% of cases, positive skin biopsy in 10%, and clinical picture alone in the final 10% of cases The only other disorder where L E cells are found is rheumatoid arthritis without multisystem disease at the time of examination Positive L E preparations have been found in 5% of this group Preliminary evidence suggests that at least some, if not all, of these cases may eventually terminate in autopsy-proved S L E

The treatment employed depends entirely upon the severity of the disease Since S L E is usually a chronic disorder subject to remissions and exacerbations, conservative treatment with rest and salicylates is used in milder forms of the disease If these are not of help or if cutaneous lesions are present, then antimalarials are added into the therapeutic regime Steroids are reserved for the severely ill patient and those with renal disease

Fifty patients have been treated with a new synthetic unsaturated corticosteroid, dexamethasone (Decadron) for as long as 15 months This hormone is 20 times as powerful on a milligram basis as hydrocortisone and 8 times as potent as methylprednisolone The initial dosage varied from 1 mg per day added to the therapeutic regimen of a patient with mild disease, partially controlled by rest, salicylates, and antimalarials to 6 0 mg per day in a critically ill patient The maximum dose utilized has been 24 mg per day for as long as three weeks The average maintenance dose was 2 7 mg per day Routine sodium restriction, potassium supplementation, and prophylactic ulcer diet were not used

A total of 94 patients had 301 serial gastrointestinal studies in order to evaluate the incidence of peptic ulcer induced by various steroids Twenty-seven persons who received dexamethasone had 58 such studies Five peptic ulcers were found in this group, and, in addition, one probable ulcer occurred making an incidence of 22% A similar occurrence rate was found in comparable groups treated with prednisone and prednisolone, methylprednisolone, and triamcinolone The majority of the steroid-induced ulcers were located in the antrum of the stomach Roentgenogram-demonstrable ulcers were found in one-half of the patients who had epigastric distress regardless of steroid employed A definite correlation was found between the dose of steroid employed and the incidence of ulceration Four of the six ulcers with dexamethasone therapy appeared in patients receiving 2 25 mg per day or more This correlates well with our findings of no ulcers in 2 patients receiving 10 mg per day or less of prednisone or its equivalent in other steroids, 13% in those receiving 10 to 19 mg per day and rising to 47% in patients taking over 60 mg per day for periods of several months A prophylactic ulcer regimen is of help in reducing these complications

The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids There was a disappearance of all the clinical and laboratory abnormalities produced by the disease with the exception of long-standing renal involvement Although there was often marked symptomatic benefit the hematological improvement was not quite as good as that produced by older corticoids

The incidence of side-effects was greater than that found in similar series treated with other hormones Edema was noted in 28% of this group, compared to a 3 to 6% incidence with methylprednisolone, triamcinolone, and the prednisteroids Hirsutism was present in 28% and insomnia was a problem in 8% of cases The other side-effects were about equally common to those previously found Proximal muscle weakness, such as that induced by triamcinolone, was not noted No electrolyte disturbances were noted Moon-face, buffalo hump, and central obesity produced by therapy with other steroids did not disappear after transfer to an equivalent dose of dexamethasone

Dexamethasone is an effective steroid in the treatment of systemic lupus erythematosus, however, because its side effects are greater than other steroids, it is not to be preferred Since it causes the accumulation of edema, it is contraindicated in the presence of cardiac or advanced renal disease Hydrocortisone is the most physiological anti-inflammatory steroid It is very predictable in its action and can be used in the majority of cases If cardiac or advanced renal disease is present, the unsaturated steroids with little sodium retaining effect and few unusual side-effects are advisable, such as prednisone, prednisolone, or methylprednisolone

Addendum

The high incidence of edema in this series raised the question whether the dexamethasone-treated group of patients was comparable to the author s series of patients given older corticoids, particularly since this was a sequential rather than a concurrent study The first significant difference noted was that the median total duration of disease in the current group was longer, namely, 96 months compared to 78 months in the triamcinolone-treated series, 72 months in the methylprednisolone-treated series, and only 28 months in the prednisteroid-treated series The second disparity was that the average maintenance dose was relatively smaller in the current group This should have decreased the incidence of edema The median total duration of continuous steroid therapy in all the groups was comparable, with the exception of the prednisteroid-treated series, being 15 5 months in the dexamethasone-treated series, 17 5 months in the methylprednisolone-treated group, 27 0 months in the triamcinolone-treated group, and 11 months in the prednisteroid-treated group

The incidence of renal involvement was similar in all series except for the triamcinolone-treated group, which only had 14% instead of 19 to 26% as in the other groups Eleven patients who developed edema in the dexamethasone-treated series had no renal involvement There was a total of 37 cases in this series without kidney damage The incidence of edema in this group is therefore 29% Black and colleagues[14] recently reported an incidence of 17% edema in a group of 23 patients with rheumatoid arthritis without cardiac or renal disease, who received smaller doses of dexamethasone than our patients The incidence of hirsutism in their series was 37%, compared to 28% in this series

The appetite-stimulating effect of dexamethasone is occasionally helpful in therapy Two patients, with systemic lupus erythematosus and severe cutaneous manifestations, required antimalarial therapy as well as steroids for control of their disease The antimalarials produced severe anorexia and weight loss which were well counteracted by the use of small doses of dexamethasone synergistically Both of these patients felt better while receiving this steroid than they had with others which they had received in the past

The poor hemoglobin response in this series may be due to small peptic ulcers which bled intermittently, but were not large enough to be visualized on x-ray examination Three patients subsequently had a marked rise in hemoglobin to normal levels after oral administration of iron Each had several negative gastrointestinal series One had hypochromic microcytic anemia, with negative stool examination for occult blood The other two had normocytic anemias, with stools which were positive for occult blood This pattern has also been noted with other steroids The corticoid-treated patient with S L E who has slightly cushingoid symptoms should have normal hemoglobin concentration unless uremia is present or there is blood loss If the patient has become moon-faced from therapy and anemia persists without significant renal damage, careful search for blood loss should be instituted

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FAMILIAL OCCURRENCE OF SYSTEMIC LUPUS ERYTHEMATOSUS

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The familial occurrence of systemic lupus erythematosus (S L E) is reported in two sisters of Italian ancestry and a mother and daughter of Mexican ancestry All four cases exhibited typical symptoms and signs of the disease The first patient was studied before the L E test was in general use, but autopsy revealed the principal microscopic criteria for S L E The other three patients had positive results of L E tests, and their conditions have been well controlled by the careful use of corticosteroids Fifteen other well documented cases in the literature bring the total reported familial instances of S L E to 19

Occasional reports of the familial incidence of systemic lupus erythematosus (S L E) have appeared in the literature The present report is concerned with its occurrence in two sisters of Italian ancestry and a mother and daughter of Mexican descent

Report of Cases

Case 1 —A female high school student of Italian parentage, aged 16 years, was seen in 1946 because of a skin eruption over the face after a severe sunburn During the next few weeks, daily elevations of temperature, joint pains, and extreme fatigue occurred Examination revealed an erythematous eruption over the cheeks, bridge of the nose, ears, and forearms A clinical diagnosis of S L E was made The patient was lost to follow-up observation until April 5, 1949, when she was admitted to the San Diego County Hospital There was a history of enlarged tender joints of the extremities in 1947, followed by stiffening and limitation of motion of the joints, fever, extreme weakness, and a loss of 35 lb (15 9 kg) in body weight during the year preceding admission Temperature was 102 F (38 9 C), pulse rate 120 per minute, and blood pressure 110/90 mm Hg Physical examination revealed emaciation (body weight 94 lb [42 6 kg]), pallor, a 'butterfly eruption over the cheeks and the bridge of the nose, and scaly, atrophic hyperpigmented lesions over the bony prominences of the extremities The joints of the extremities showed extensive wasting, slight flexion deformity, and limitation of motion There was generalized enlargement of lymph nodes and of the spleen and liver A systolic murmur was well localized over the apex of the heart No other abnormal findings were present

L E clot tests were not performed The serum albumin level was 2 4 Gm % and that of serum globulin 4 8 Gm % Reactions to the blood Kahn and Kolmer-Wassermann tests were positive The sedimentation rate was 38 mm in 30 minutes (Cutler method) The hemoglobin level was 5 5 Gm % and the leukocyte count 6,000 per cubic millimeter The differential count was normal Urinalysis revealed a moderate amount of albumin but was normal otherwise An x-ray of the chest, roentgenographic skeletal survey, and an electrocardiogram revealed no abnormalities The patient's condition deteriorated gradually with remissions and exacerbations, and she died on June 5, 1950

Autopsy findings were summarized as follows A review of the autopsy slides showed the principal microscopic criteria for disseminated lupus erythematosus The mitral valve showed atypical verrucous endocarditis, and the heart showed focal myocarditis The spleen showed connective tissue arranged in concentric rings about small arteries simulating onion rings In addition, about 20% of the glomeruli of the kidneys were diseased and many of these showed an atypical 'wire loop" appearance None of the tissue showed any accumulation of hematoxylin bodies

Case 2 —The sister of the patient in case 1 was admitted to San Diego Mercy Hospital on Aug 27, 1957, at the age of 15 years, because her mother realized that her symptoms were similar to those of the sister who had died in 1950 Diffuse pigmentation of the cheeks had followed sunburn at the age of 4 years and had become more prominent after each exposure to sunlight However, the patient had been well until one month before admission, when the eruption increased and involved the bridge of the nose This was accompanied by fatigue and vague joint pains There was no elevation of temperature Important physical findings were an erythematous eruption over the cheeks and the bridge of the nose, enlargement of the postauricular and posterior cervical lymph nodes, and slight swelling of the fingers No heart murmurs were heard and the blood pressure was 120/88 mm Hg The liver and spleen were not enlarged

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From the Scripps Clinic and Research Foundation (Dr Marlow) the Rees Stealy Clinic (Dr Peabody) and the Mercy and San Diego County hospitals (Dr Nickel)

The result of the L E clot test was ambiguously positive The serum albumin level was 4 4 Gm % and that of serum globulin 4 7 Gm % Reactions to the blood Kahn and Kolmer-Wassermann tests were positive Sedimentation rate was 34 mm per hour (Wintrobe) The hemoglobin level was 10 Gm % and the leukocyte count 5,300 per cubic millimeter The differential count was normal Urinary findings were not abnormal Roentgenographic findings of the chest and hands were within normal limits No treatment was given

The patient was discharged on Aug 28, 1957, but was readmitted on Oct 17, 1957, with complaints of sore throat, severe pains in the joints of the extremities, and a temperature ranging from 102 to 103 F (38 9 to 39 4 C) Chloroquine phosphate, given in increasing doses from 250 to 750 mg daily, produced no relief All symptoms and signs disappeared when prednisone, 40 mg daily, was substituted for chloroquine She was discharged from the hospital on Nov 5, 1957 The dose of prednisone was decreased gradually to 20 mg daily, but symptoms reappeared when further reductions in dosage were attempted A severe exacerbation of symptoms required readmission and administration of increased doses of corticosteroids in April, 1958, however, the amounts were again reduced gradually, and the patient has required an average of 7 5 mg of prednisone daily during the past year She is able to attend school without undue fatigue The result of the L E clot test was positive on July 13, 1959

Case 3 —A Mexican housewife, aged 33 years, was admitted to San Diego Mercy Hospital on Nov 21, 1956, with a history of chills, fever, joint pains, left-sided chest pain, and pain in the right upper abdominal quadrant for about two months after a trip to the beach Physical examination revealed an acutely ill, dyspneic, and slightly cyanotic woman whose temperature was 101 F (38 3 C) No skin eruption was present There was tenderness over the muscles and joints of the extremities and pain on motion of the joints The appearance of the joints was normal The percussion note was dull, and breath sounds were decreased over the entire right side of the chest and, to a lesser extent, over the lower half of the left side of the chest The heart was slightly enlarged and a systolic gallop rhythm was present, but no murmurs were heard The blood pressure was 130/80 mm Hg There was marked tenderness on palpation of the right upper quadrant of the abdomen, and the liver was palpable 4 cm below the right costal margin The spleen was not palpable

The result of the L E clot test was positive More than 50% of the neutrophils showed the L E phenomenon The serum albumin level was 3 1 Gm % and that of serum globulin 5 8 Gm % The reaction to the blood Kahn test was negative The uncorrected sedimentation rate was 62 mm per hour (Wintrobe) The hematocrit reading was 30%, hemoglobin level 11 1 Gm %, and the leukocyte count 5,250 per cubic millimeter The differential count was normal Urinalysis revealed 1 or 2 leukocytes per high-power field and occasional granular casts, but no other abnormal findings The blood nonprotein nitrogen level was 67 mg % An x ray of the chest showed bilateral pleural effusions and slight enlargement of the heart An electrocardiogram revealed inversion of T waves in all leads except V_1 and aVR These findings were interpreted as suggestive of pericarditis

All symptoms disappeared within 48 hours during the administration of 120 mg of prednisolone daily Prednisone was substituted for prednisolone and the dose was reduced gradually The patient is now asymptomatic on a regimen of 6 mg of prednisone twice daily

The patient's daughter, aged 6 years, and her son, aged 11 years, have negative results of the L E clot test

Case 4 —The mother of the patient in case 3, aged 62 years, developed bilateral pericardial effusions and a possible pericardial effusion in Mexico, in 1951 They were accompanied and followed by severe joint pains and extreme weakness The patient became much worse when she learned that her daughter had "lupus" in November, 1956 She was acutely ill with a temperature of 101 2 F (39 C) at the time of admission to the Scripps Clinic and Research Foundation on June 21, 1957 On physical examination, the patient appeared pale and ill There was no skin eruption Atrophic changes of the hands gave the appearance of rheumatoid arthritis but other joints did not appear abnormal Axillary lymph nodes were enlarged to average diameters of 1 5 cm A grade 2 systolic murmur was present over the left precordium, maximal at the apex and not transmitted No diastolic murmur was heard The blood pressure was 140/80 mm Hg The spleen was palpable 4 cm below the left costal margin The liver was not enlarged

The results of the L E clot, rotation, and ring tests were positive The serum albumin level was 2 7 Gm % and that of serum globulin 6 Gm % Results of the blood Kahn and Venereal Disease Research Laboratory tests for syphilis were negative The uncorrected sedimentation rate was 62 mm per hour (Wintrobe) The hematocrit reading was 32%, hemoglobin level 9 6 Gm %, and the leukocyte count 4,100 per cubic millimeter The differential count was normal The result of urinalysis was normal and the blood urea nitrogen level was 20 mg % An x-ray of the chest revealed no abnormalities A roentgenographic bone survey revealed slight osteoporosis of the bones of the hands and wrists, but the skull, lumbosacral spine, and hips were normal An electrocardiogram showed a slight oblique depression with a straight-line contour in lead V_4, but no other abnormalities

The patient became asymptomatic within 24 hours on a regimen of 80 mg of prednisolone daily Prednisone was substituted for prednisolone and the dose was reduced gradually With the exception of a complaint of weakness, the patient is asymptomatic on therapy with 4 mg of prednisone daily

Comment

In 1956, Glagov and Gechman [1] reported the occurrence of fatal disseminated lupus erythematosus in an American woman aged 44 years, who had been born in Russia, and her 18-year-old daughter who had been born in the United States They reviewed five previously reported instances of familial occurrence but considered only three of them to be sufficiently well documented to be acceptable examples [2]

In 1957, Agranat, Bersohn, and Lewis [3] reported familial disseminated lupus erythematosus in a caucasoid woman aged 30 and her married sister aged 45 years The first patient had been observed for five years for arthritis before the diagnosis was made She was reported to be doing well on chloroquine phosphate therapy The sister had a history suggestive of rheumatoid arthritis for six years before the diagnosis of disseminated lupus was made She was also said to be making excellent progress on chloroquine therapy at the time of the report

In 1957, Leonhardt[4] reported S L E in 3 of 14 siblings They had high gamma globulin levels in the blood, and five other siblings had marked elevations of gamma globulin without evidence of S L E The author suggested that there may be an inherited tendency to hypergammaglobulinemia leading, in some instances, to S L E

In 1958, Wagenhals and Burgeson [5] reported fatal S L E in identical twins Autopsies were not obtained, but the cases are well documented These authors reported that they had been able to find only one previous report [2b] of S L E in identical twins

In 1954, Bridge and Foley [6] reported the placental transfer of the L E factor from a 20-year-old woman with known S L E to her normal male offspring L E cells could be demonstrated in the mother and child at birth They persisted in the baby for seven weeks but disappeared by the age of 4 months The authors were unable to demonstrate antibodies, which precipitate the L E factor in rabbits injected with the gamma globulin factor, from the baby's blood The authors did not suggest that the baby had or would develop S L E They mentioned another instance of their demonstration of the L E phenomenon in the cord blood of an infant born to a 26 year-old woman with S L E in a footnote after their paper had been submitted for publication

In 1957, Berlyne, Short, and Vickers [7] reported transmission of the L E factor from two mothers with S L E to their newborn infants As in the case reported by Bridge and Foley,[6] L E cells disappeared from the infant's blood after seven weeks

In 1958, Burman and Oliver [8] reported the presence of L E cells in the blood from the umbilical vein of a fetus aged 20 weeks at the time of a therapeutic abdominal hysterotomy performed on a 25-year-old mother who had S L E

We have been able to select 15 well-documented instances of familial S L E from the literature and add the four cases described in this report In 1959, McKusick [9] had discussed S L E in a report on "Genetic Factors in Diseases of Connective Tissue" He referred to reports of the familial incidence of discoid lupus and S L E and seven additional instances of familial S L E which had not been reported in detail

Because of increasing reports of the incidence of familial S L E, a report of familial hypergammaglobulinemia and S L E, and reports of the placental transmission of the L E factor, we believe that attention should be drawn to the possibility that hereditary factors may play a role in the etiology of S L E

Summary

Systemic lupus erythematosus (S L E) occurred in two sisters of Italian ancestry and a mother and daughter of Mexican descent Fifteen other well-documented instances of the familial incidence of S L E are reported in the literature In one report, hypergammaglobulinemia was present in 8 of 14 siblings, 3 of those siblings had S L E The literature also contains five reports of placental transmission of the L E factor These data suggest the possibility that hereditary factors play a part in the etiology of S L E

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SURGICAL TREATMENT OF MITRAL STENOSIS BY OPEN TECHNIQUE

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Development of operations of the closed type for the correction of mitral stenosis was an important pioneer step The open type, however, makes it possible to perform precise dissections that have never been accomplished with nearly the same degree of effectiveness by the closed technique in the past Operations by the open technique were done in 44 patients Among the 22 who had primary mitral stenosis there were 2 operative deaths (9%) Among the remaining 22, who had combined mitral lesions, there were 4 operative deaths (18%) About 15% of the stenotic mitral valves at operation are found to be so severely damaged by disease that little benefit can be anticipated from either closed or open operation For reliable evaluation of results it is necessary to obtain objective data sufficiently long after operation rather than clinical impressions during the immediate postoperative period

Much has been accomplished in the surgical treatment of mitral stenosis since the pioneering efforts of Bailey,[1] Harken and associates,[2] and Baker, Brock, and Campbell[3] 10 years ago Many patients have been greatly relieved by such operations Evaluation studies performed after a number of years, however, have been less favorable than those performed relatively soon postoperatively This is illustrated in the findings of Neptune and Bailey,[4] who reported that the condition of 89 8% of the patients who survived operation improved (78 6% of the initial group), whereas of 60 patients operated on five years or later only 25% were clinically cured and another 33 3% rehabilitated[5]

Background

Most evaluation studies have shown disappointingly little correlation between clinical improvement and roentgenographic, electrocardiographic, or hemodynamic improvement[6] In most instances there has been even less correlation between clinical and hemodynamic improvement In those reports stating that clinical improvement parallels hemodynamic improvement, actually only a small percentage (20-30%) of the patients returned to normal after correction by the closed technique, and this occurred primarily in patients in class II and in patients with a mild condition in class III Unfortunately, most of the evaluation studies in the past did not include complete hemodynamic tests but were frequently incomplete in that pressure studies, with and without exercise, and determinations of pulmonary capillary-wedge pressures were either not performed or not reported The condition of some of the patients which showed initial improvement later deteriorated, and in some in whom catheterization studies were performed early it later improved Because of the lack of correlation between clinical and objective findings, physiological studies were largely discounted In our studies, those patients with clinical improvement but no significant hemodynamic improvement were the ones who later again showed signs and symptoms of valvular obstruction whereas no patient in whom the hemodynamic findings returned to normal had subsequent trouble It was also apparent that those patients with advanced pulmonary vascular changes took longer to reverse their hemodynamic findings, and rarely had reversal to the same degree as those with less severe changes

Even though, admittedly, the surgical relief of mitral stenosis by the closed technique was a pioneering event in heart surgery that provided relief for many patients, it is fraught with shortcomings Its main virtues are its simplicity and ease of performance Failure of accomplishment, however, was high in patients with associated regurgitation, severe calcification, and subvalvular stenosis In a survey of cardiac surgeons in 1957,[7] over 50% thought that the technique could be improved Many surgeons have sought means other than the originally described closed techniques to improve their results

Success in the surgical relief of mitral stenosis entirely depends on (1) the status of the myocardium affected by rheumatic fever, as well as chronic strain from valvular obstruction, (2) the status of the stenosed valve—be it fibrotic but pliable, heavily scarred with subvalvular stenosis from matting together of the leaflets, chordae tendineae cordis, and papillary muscles, or heavily calcified, and (3) the status of the pulmonary vasculature

Other lesser factors are the age of the patient, the chronicity of the obstruction, and the presence of atrial fibrillation and atrial thrombosis Factors (1) and (3) are somewhat under the control of the physician who has followed the patient's course over a number of years Obviously, surgical techniques should not be criticized for failure to pro

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From the medical and surgical services of St Vincent Charity Hospital vide relief if the physician allows the patient to progress to the state of irreversible pulmonary hypertension and chronic myocardial failure

Surgical Problem

The relief of mitral stenosis is a surgical problem All surgeons agree that the greater the degree to which valvular function is restored, the greater the likelihood of improvement Most surgeons also agree that poor results or failure of improvement from a technical point of view largely depend on (1) the presence or degree of subvalvular fusion of the chordae papillary structures, (2) the degree of calcification, (3) whether or not regurgitation is produced or aggravated, and (4) the completeness of the correction (which, even at its best, is only partial—a normal valve is never obtained)

There is no question that the experience of the operator is a large factor in the incidence of postoperative success and undoubtedly accounts to a great degree for the variation in comparative analyses in varying series However, with the passage of time and the accumulation of experience, surgeons for the most part began to realize that many times, for one reason or another, they had to be content with attaining an opening of the valve less than optimal or that they could not open a valve further because of regurgitation, and that their percentage as a whole of obtaining really maximal size and return of optimal valvular function with the closed technique, without causing significant regurgitation, was considerably less than desirable and comprised only between 40 to 70% of the valves explored

Surgical Opinions—To quote only a few of the surgical opinions, the following excerpts are presented Bailey, Hirose, and Morse[8] held that "Complete mobilization of the stenotic mitral valve has been achieved in the past only in those few individuals in whom the leaflets have become but slightly deformed and lightly cross-adherent, the chordo-papillary supports remaining relatively free and flexible Such patients make up no more than 10 to 12 percent of those who seek surgical aid for mitral stenosis The remaining 80 or 90 percent of patients have what amounts pathologically to a fibrous or fibrocalcific stricture of the left atrioventricular passageway The benefit initially achieved by commissurotomy in these patients who have advanced pathologic changes in the valve has been of limited degree Unless a considerable amount of flexibility persists in the leaflets and in the subvalvular supporting structures, relatively little mobility and even less function will be restored to the valve"

Bailey and Hirose[9] wrote, Because of increasing dissatisfaction with even the improved commissurotomy procedure possible by the right-sided approach, the described new concept of a method for complete reconstitution of valve action was born In spite of the evolution of this concept of relinging of the septal leaflet which would seem to approach the surgical ideal, we have not always succeeded in accomplishing this objective in practice a completely satisfactory mobilization was accomplished in only 70%"

Ellis, Harken, and Black[9f] stated, "A group of 228 patients who deteriorated after substantial improvement persisting at least one year were analyzed Factors that were found in a significantly higher percentage than in patients who maintained their improvement were mitral insufficiency, an unsatisfactorily performed valvuloplasty, and clear-cut rheumatic fever occurring since operation" Dively and associates[10] maintained that "In only 40% of the patients was it possible to do a complete commissurotomy Mitral insufficiency, or incomplete commissurotomy accounted for 70% of the poor results"

The intent of our contribution is in no way meant to detract from the benefits derived from the closed technique of surgical correction in helping about 50% of the patients surviving operation, instead, it is hoped to point out that the other 50% of the patients with valvular disease, who have more severe pathological changes, such as subvalvular stenosis, extensive calcification, or associated regurgitation, have been the group in whom the rate of operative and late deaths has been high and the likelihood of improvement less

Closed Versus Open Technique—Our interest in the increased benefit obtainable by the open heart–direct vision technique, in which extracorporeal circulation by means of a pump oxygenator is used, resulted from reoperation on two patients who, respectively, had been operated on six and seven years previously Both were patients in class III whose condition, after operation, was considered to be greatly improved clinically, which correlated with hemodynamic improvement as shown by cardiac catheterization studies

The first patient was operated on in March, 1951 Preoperative pulmonary artery studies showed pressure in the pulmonary artery to be 58/18 mm Hg Four years later catheterization studies were again performed, and the pressure was found to be reduced to 42/20 mm Hg At this time it was thought that her condition was still greatly improved Three years later, in March, 1958, she was again showing signs and symptoms of mitral obstruction Catheterization data obtained at this time showed no increase in pulmonary artery pressure at rest, but with exercise this became elevated to 62/32 mm Hg, and the pulmonary capillary pressure was 32/21 mm Hg It was thought that perhaps further improvement could be obtained if she were reoperated on by the direct-vision technique Catheterization studies were again performed 10 months postoperatively Pulmonary artery pressure was now reduced to 21/6 mm Hg (see table) and did not increase significantly with exercise The pulmonary capillary pressures had decreased to 12/6 mm Hg

The second patient had been operated on in January, 1952, with a preoperative pulmonary artery pressure of 67/37 mm Hg and a pulmonary capillary pressure of 40/25 mm Hg This patient's condition was also thought to be markedly improved Five years later he was catheterized again Though the pressures had fallen considerably they were still significantly elevated The pulmonary artery pressure was 51/21 mm Hg at rest and 75/43 mm Hg with exercise The pulmonary capillary pressure had fallen to 28/21 mm Hg Two years later he was catheterized again, with evidence that the mitral obstruction was becoming progressive At this time, in February, 1958, the pulmonary artery pressure was 55/20 mm Hg at rest and rose to 90/55 mm Hg with exercise The pulmonary capillary pressure had increased to 30/20 mm Hg This patient was also reoperated on by the open technique Nine months later catheterization studies showed that at this time there was a significant improvement in cardiac hemodynamics compared to the pressures obtained after operation by the closed technique Both these patients recognized the considerably greater improvement after this correction of their mitral obstruction than that obtained after use of the closed technique Both these patients had leathery fibrotic valves, with some subvalvular stenosis

Results of Hemodynamic Catheterization Studies in Patient with Mitral Stenosis Corrected with Both Closed and Open Valvuloplasty

	Pressure Mm Hg				
			Pulmonary Arterial		Pulmonary Capillary
	Atrial	Ventricular	Rest	Exercise	
Closed Operation March 1951					
Preoperative March, 1951	8/4	58/2	58/18		
Postoperative May 1955	5/0	44/0	42/20		
Open Operation, March 1958					
Preoperative March 1958	9/2	42/-2	42/18	62/32	32/21
Postoperative, Jan, 1959	3/1	24/0	21/6	31/15	12/6

With this evidence of the increased benefit obtainable by the open technique, it was thought that greater attention should be given to objective studies obtained by cardiac catheterization rather than to discount such evidence, as many others had, in the belief that, as long as the patient admitted to feeling improvement, the surgeon and the cardiologist should be satisfied

Hemodynamic Results Obtained by Closed Technique—On the basis of these data, we again examined the hemodynamic findings of patients in classes III and IV, who had been previously operated on by the closed technique, to determine how many obtained similar improvement It is these groups, and particularly the patients in class IV, who had in the past obtained the poorest results after correction by the closed technique

Unfortunately, not as many patients as would have been desirable had complete preoperative and postoperative cardiac catheterization studies There were 38 patients with data sufficiently complete to draw certain deductions Six patients were studied from one to two years postoperatively, and 32 patients from two to seven years postoperatively In only 12 of the 38 patients (31 6%) had the pulmonary artery pressures fallen to below 35 mm Hg at rest, however, with exercise 8 of these patients had pressures over 50 mm Hg This would indicate that some degree of mitral stenosis or pulmonary vascular sclerosis still existed Data were obtained for 28 patients after exercise In 22 (78 6%) of these, pressures became elevated to 50 mm Hg or more, and in 12 (42 9%) to over 60 mm Hg

This would suggest that, at least hemodynamically, not over 22% of the patients in classes III and IV returned to within essentially normal limits In other words, about 80% of these patients in classes III and IV still had some evidence of either mitral stenosis or pulmonary vascular sclerosis based entirely on objective findings from one to seven years after their operation by the closed technique This is a considerably lower improvement rate than that based on clinical appraisal alone Many of these patients have remained clinically improved over this period, although they still show elevated pulmonary artery and pulmonary capillary wedge pressures Evidence and impressions based entirely on hemodynamic findings obtained by cardiac catheterization obviously are not entirely reliable but at least should be more accurate than analysis based on clinical impressions alone To even the most skeptical observer such evidence, however, would suggest that perhaps patients in classes III and IV could obtain greater hemodynamic improvement in the future by better techniques than the closed techniques afforded them in the past We have purposely not included patients in class II, for in them the valve invariably is more suitable for surgical correction by the closed technique This impression is not entirely true, however, for in the past, some of our patients in class II (a classification based on signs and symptoms and not on valvular disease) have had subvalvular stenosis which could not be completely corrected by the closed technique

Selection of Patients

On the basis of this evidence that clinical appraisal was not as accurate as one based on objective findings, with the knowledge that certain patients with leathery fibrotic valves with some subvalvular stenosis could be afforded greater relief through correction of their valvular deformity by the open than had been obtained after use of the closed technique, and with the knowledge that no one can accurately foretell the possible valvular disease which may be encountered at surgery, all patients requiring correction for mitral stenosis in the past two years have been prepared preoperatively to have their correction performed under direct vision with the pump oxygenator As time goes on, mitral stenosis is being corrected in an increasing percentage of patients by the open as com pared to the closed technique In our opinion, these should be considered not as competing but as complementary techniques, each to be used when best indicated The mitral valve in all these patients was approached from the right side If a satisfactory opening of the mitral valve can be obtained by the closed technique, nothing further is required However, if a satisfactory correction cannot be obtained, if there is an associated regurgitation, or if regurgitation is produced during the operative maneuver, the laboratory is notified to draw blood from prearranged donors, the cannulations are performed, and the correction is then carried out under direct vision Knowing what can be accomplished in the way of surgical correction, our criteria for a satisfactory opening by the closed technique is becoming more and more critical It must be emphasized that the availability of a heart-lung machine and the fact that the correction is attempted by the open rather than the closed technique does not mean that such a correction will necessarily be better but only that, with proper experience, better correction with the open technique is possible

Analysis of Patients During the past two years, mitral stenosis in 44 patients has been corrected by the open technique Of these patients, 22 had primarily mitral stenosis and 22 had an associated mitral regurgitation, as judged at the time of the operative procedure Ten of the patients, three with primarily mitral stenosis and seven with combined lesions, had been operated on previously in six different surgical centers Of the 22 patients with combined lesions, 19 were in class IV and the other 3 in class III Of the 22 patients with stenosis primarily, 14 were in class IV and the other 8 in class III

Operative Data

Mortality —Two operative deaths occurred among the 22 patients (8 patients in class III and 14 patients in class IV) with primarily mitral stenosis, an operative mortality of almost 10% Both of these deaths occurred in patients with extensively destroyed calcified valves There were four operative deaths (18%) among the 22 patients with combined lesions (3 patients in class III and 19 patients in class IV), for an over-all operative mortality of 13% The four deaths in this group occurred in patients with extensive valvular and subvalvular fibrocalcific disease in whom little in the way of hemodynamic improvement could be obtained even by the open technique However, we believe that, with subsequent greater experience, perhaps two of these patients could now be afforded some benefit This low operative mortality compares favorably with the operative mortality obtained by the closed technique in such patients Again, it must be emphasized that this is a selected group, comprised of patients with more severe degrees of pathological changes, since those patients with less severe disease were operated on by the closed technique All 10 patients previously operated on by the closed technique survived and were greatly benefited by the surgical correction At the time of writing, about 80% of the patients at the time of the digital exploration, or after attempts at surgical correction by the closed technique, have either insufficient valvular correction or associated complicating factors which, in the opinion of the operator, are more suitably corrected by the open technique This, in our minds, is a forward step in the over-all handling of patients with mitral stenosis

Techniques —Those patients in whom the pathological process is largely confined to the leaflet aspect of the valvular mechanism can, in most instances, obtain effective correction of mitral stenosis by either technique Thirty-six patients (81%) in this series had varying degrees of subvalvular stenosis to the extent that in some there was complete fusion of the papillary muscles with the immobile scarred leaflets With use of the closed technique, 'blindly," it would have been impossible in such instances either to determine or effectively to develop a cleavage plane in the proper position without tearing or cutting the musculotendinous support to one or the other of the leaflets resulting in a flail valve A small superficial incision is made over what is anatomically supposed to be the site of the pathological obliteration of the leaflets This incision is carried down to the fused papillary muscles, which in turn are split to their ventricular attachments Care is exercised that each leaflet have sufficient supporting musculotendinous structures Unless this subvalvular stenosis is relieved, little, if any, benefit will be obtained This sub valvular dissection is most precise and difficult even under direct vision and, in our experience, has never been accomplished with nearly the same degree of effectiveness by the closed technique in the past

It should also be emphasized, contrary to past teachings, that the mitral valve is not truly a bifid valve but rather a sleeve valve in which there is a large anterior leaflet, a smaller posterior leaflet, and two even smaller septal and mural leaflets which prevent regurgitation at these sites This concept is not new but has been described in most textbooks on anatomy It has also been taught that the obliterated commissure (which is actually a pathological and not an anatomic condition) should be well opened to the annulus This teaching probably was of little concern in the past, for in most instances it would have been impossible to accomplish by the closed technique It is possible, however, that in those instances in which it was accomplished, it was responsible for surgically produced mitral regurgitation in some patients However, under direct vision, it is possible ill-advisedly to sever the valve tissue out to the annulus, which in turn destroys the integrity of the mitral valve, allowing the anterior and posterior leaflets to separate and incompetency to develop

This dissection should never be carried nearer than 2 mm to the annulus, and in some instances even less.

It is disconcerting to find that still about 10% of the more severely stenotic valves are so pathologically destroyed that little, if any, benefit can be obtained by either the closed or the open technique. This group of patients accounts for the greater proportion of the operative mortality with use of either the open or the closed technique. To obtain benefit in the future, these patients must have complete valvular replacement in the form of artificial prosthesis. Such an artificial valve has been developed in our laboratory, fashioned after the normal anatomic valve with leaflets and chordae tendineae. Preliminary laboratory and clinical observations of this artificial valve appear most promising.

Postoperative Evaluation

Of the 38 patients who survived operation, one subsequently died (eight months postoperatively) from myocardial failure. This was a patient with extensive subvalvular stenosis in whom it was impossible to obtain an ideal opening even by the open technique. Even though cardiac catheterization studies performed six months postoperatively showed reduction in the pulmonary artery pressure from 105/35 to 68/28 mm Hg and in the capillary pressure from 48/21 to 22/18 mm Hg, chronic myocardial failure still existed and was undoubtedly one of the causes contributing to death.

Obviously, evaluation studies obtained too soon postoperatively are meaningless. The course of 24 patients, however, has been followed for from six months to two years postoperatively. Judged clinically, 21 (87.5%) have obtained excellent improvement. Two (8%) have obtained moderate improvement, to the extent of being no longer in persistent myocardial failure. In one patient there has not been any significant clinical improvement, even though the pulmonary artery pressure has fallen from 50/16 to 37/20 mm Hg and the pulmonary capillary pressure from a mean of 27 to 24 mm Hg. This patient's status is six months postoperative. We believe that failure of improvement in this patient is due primarily to left ventricular failure. Again, a more significant evaluation must wait until all these patients have been recatheterized.

Of the 10 patients who had been previously operated on at various clinics, including our own, 3 patients with mitral stenosis primarily were previously operated on by us two, six, and seven years previously. At that time it was thought that satisfactory opening of the stenosed valve had been obtained. However, judging in retrospect from what can be accomplished by the open technique, one must say that the operative correction obtainable at that time by the closed technique was considerably less than ideal. All these patients have obtained excellent improvement, with return of their hemodynamics to normal. Of the seven patients previously operated on for stenosis combined with other lesions, two had had their valves lacerated elsewhere from use of the commissurotomy knife, with resultant regurgitation and cardiac failure. In the five other patients with subvalvular stenosis little, if any, benefit was derived from the closed technique. All these patients have obtained excellent improvement. Nine of the patients have now been catheterized from six months to two years postoperatively, with a reduction in hemodynamics far superior to that obtainable with the closed technique. Six of these patients now have pulmonary artery pressures ranging from 21 to 35 mm Hg, pressures in the other three are 37, 41, and 42 mm Hg respectively.

Comment

Much has been accomplished during the past 10 years in the surgical treatment of mitral stenosis by the closed technique. This technique is particularly attractive because of its simplicity, ease of performance, and low operative mortality. Increasing evidence, however, points to the fact that frequently the improvement so obtained has been only partial and temporary. Furthermore, its potential for accomplishment is limited in the presence of subvalvular stenosis, valvular calcification, and regurgitation. In contrast, surgical correction by the open technique is unquestionably more complicated, and the ability to recognize and properly correct the presenting pathological factors necessitates a completely new surgical orientation of the pathological anatomy, used primarily in the surgical correction of types of defects poorly corrected by the closed technique. Each technique has its field of usefulness.

The superiority of the open technique over the closed method in more severely afflicted patients is amply demonstrated by the more complicated type of defect that can be successfully corrected, the marked improvement in 10 patients who had been previously operated on by the closed technique in various surgical clinics, and the over-all improvement in postoperative in hemodynamic findings in those studied. There still exists, however, a group of patients with destroyed valves in whom little in the way of clinical or hemodynamic improvement was obtained by either the open or the closed technique which comprises most of those dying early in the postoperative period. In the future, success in these patients will depend on the successful development and application of artificial valves. Last, but not least, additional over-all improvement will be forthcoming in the surgical treatment of patients with mitral stenosis if they are operated on before they develop advanced pulmonary vascular sclerosis and chronic myocardial failure.

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EFFECT OF 14-HYDROXYDIHYDROMORPHINONE ON RESPIRATION

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and
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The effect on respiration of 14-hydroxy dihydromorphinone was tested in 16 patients, 6 healthy young men, and 10 older patients with cardiovascular, pulmonary, or hepatic disease After subcutaneous injection of 1 5 mg of the drug (said to be equivalent to 15 mg of morphine) changes in minute ventilation, respiratory rate, and tidal volume were determined and related to oxygen saturation, carbon dioxide tension, and pH of arterial blood Definite depression of respiration and a marked reduction in sensitivity of the respiratory center to carbon dioxide stimulation were observed in all 16 subjects The respiratory depression was subclinical in the young, normal subjects but was usually apparent in the 10 older patients Caution must be exercised with doses of this amount in elderly persons and in patients such as those with cardiovascular, pulmonary, or hepatic disease, who are known to be sensitive to central nervous system depressants

A synthetic morphine derivative, 14-hydroxydihydromorphinone (Numorphan), has recently been introduced It is said to provide analgesia superior to that provided by morphine and to be associated with a reduced incidence of undesirable side-effects particularly respiratory depression[1] A drug with potent analgesic properties and minimal respiratory depressant effect would be an important addition to the therapeutic armamentarium A study was undertaken, therefore, to evaluate the effect of 14 hydroxydihydromorphinone on respiration

Material and Methods

Sixteen patients were studied (table 1) Six were normal young men The other 10 were older patients with cardiovascular, pulmonary, or hepatic disease None of the group were narcotic addicts All subjects were studied in a basal state A Cournand needle was inserted into a brachial artery and left in place throughout the test period Specimens of arterial blood could then be collected periodically without disturbing the subject, who was in a

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Residents in Medicine Veterans Administration Hospital (Drs Resnick and Berkowitz) Staff Physician Veterans Administration Hospital and Instructor in Medicine Temple University Medical School (Dr Rodman) Chief Medical Service Veterans Administration Hospital and Professor of Clinical Medicine Temple University Medical School (Dr Close) supine position during the procedure The resting minute ventilation was determined by collecting the expired gas for a measured period of time in a 125 liter Tissot gasometer while the subjects breathed compressed air The respiratory rate was recorded on a moving kymograph Specimens of arterial blood were drawn during the gas collection period and analyzed for oxygen content, oxygen saturation, carbon dioxide content, and pH The carbon dioxide tension was calculated from the line charts of Sendroy and van Slyke and from the Henderson-Hasselbalch equation[2] Samples of expired air were analyzed for oxygen, carbon dioxide, and nitrogen content The carbon dioxide output, oxygen uptake, respiratory quotient, and basal metabolic rate were calculated The details of the techniques used in our laboratory have previously been reported[3] In addition to these basal determinations, the six normal subjects were permitted to breathe first 4 17 and then 5 63% carbon dioxide in air Each gas concentration was administered long enough to permit the maximum stimulatory effect of carbon dioxide on the respiratory center The minute ventilation was then measured, and specimens of arterial blood were drawn during the inhalation of each of the two concentrations of carbon dioxide A graph of these data was constructed for each subject (fig 1) relating changes in the partial pressure of carbon dioxide in the arterial blood to changes in minute ventilation

TABLE 1—*Data in Subjects in Whom Respiratory Depressant Effects of 14-hydroxydihydromorphinone Were Studied*

Diagnosis	Patients, No	Average Age, Yr	Age Range, Yr
Normal	6	35 5	29-40
Cardiovascular disease	4	68 8	60 76
Cerebral arteriosclerosis	2		
Arteriosclerotic heart disease	2		
Pulmonary disease	4	55 8	29 69
Obstructive emphysema	2		
Bronchogenic carcinoma	1		
Bronchial asthma with bullae	1		
Hepatic disease	2	50 5	40 52
Severe atrophic cirrhosis	1		
Mild atrophic cirrhosis with polycythemia vera	1		

After completion of the basic studies, 1 5 mg of 14-hydroxydihydromorphinone was administered subcutaneously This dose is said to be equivalent to 15 mg of morphine Forty minutes later all of the tests were repeated It was then possible not only to evaluate changes in minute ventilation, respiratory rate, and tidal volume induced by the administration of 14-hydroxydihydromorphinone but also to relate these variations to changes in oxygen saturation, carbon dioxide tension, and pH of arterial blood In the normal subjects it was possible to correlate the effect of 14-hydroxydihydromorphinone on the response of the respiratory center

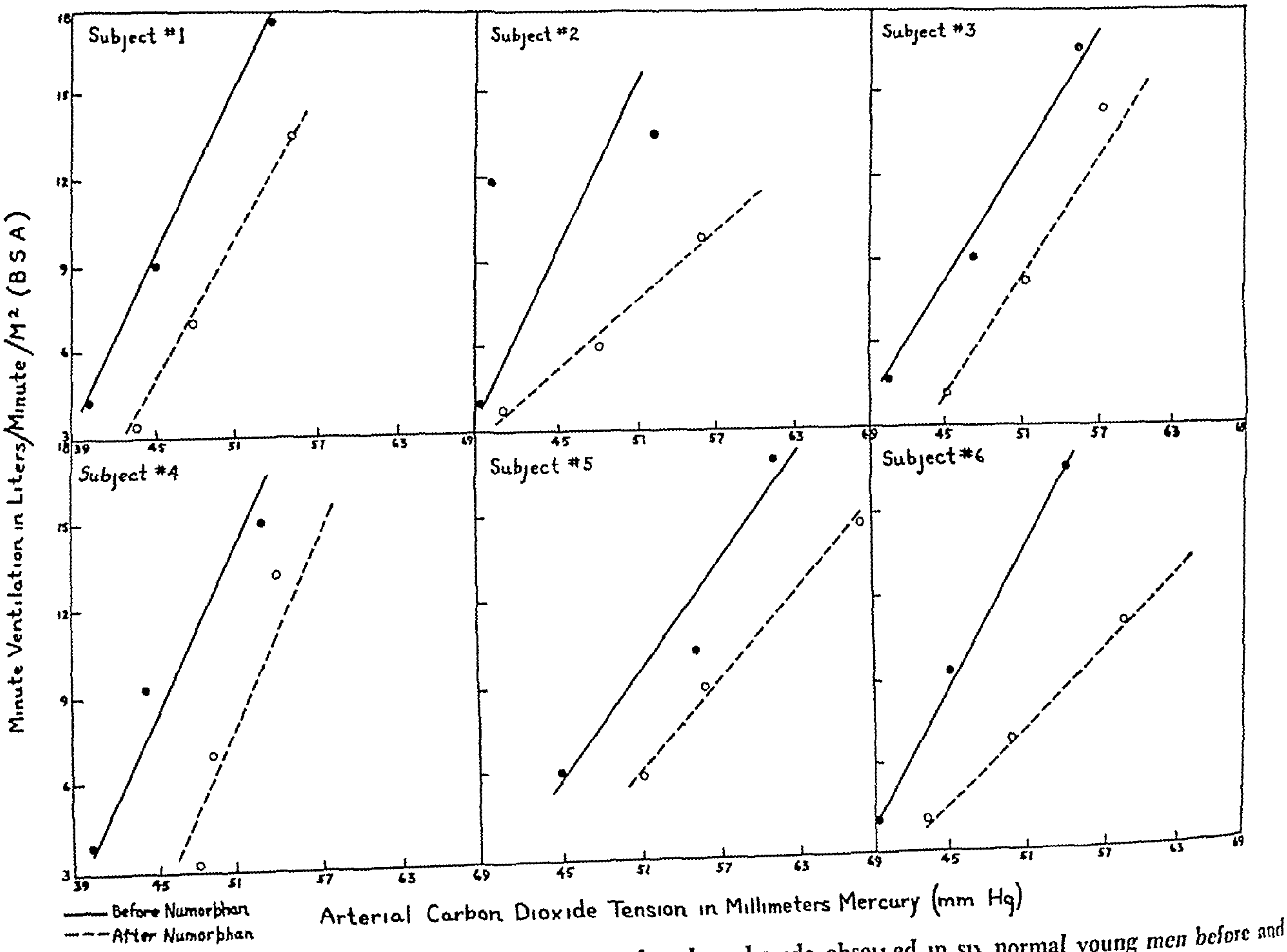

Fig 1—Ventilatory response to increased concentrations of carbon dioxide observed in six normal young men before and 40 minutes after subcutaneous administration of 1 5 mg of 14-hydroxydihydromorphinone (Numorphan)

with changes in carbon dioxide tension over a wide range of partial pressures

In addition to the above studies, the cardiac output was measured by a dye dilution technique with T-1824 Evans blue dye in five of the six normal subjects before and after the administration of 14-hydroxydihydromorphinone

TABLE 2 —*Effect of 1 5 Mg of 14-hydroxydihydromorphinone on Minute Ventilation, Arterial Carbon Dioxide Tension, and Arterial pH of Six Normal Subjects*

	Administration of 14 hydroxydi hydromorphinone	
	Before	After
While breathing air		
Minute ventilation (l /min /m)	4 45	4 17
pCO (mm Hg)	41	45
pH	7 40	7 36
While breathing 4 17% CO in air		
Minute ventilation (l /min /m)	9 76	7 39
pCO (mm Hg)	46	50
pH	7 35	7 32
While breathing 5 63% CO_2 in air		
Minute ventilation (l /min /m)	16 0	12 9
pCO (mm Hg)	55	58
pH	7 30	7 27

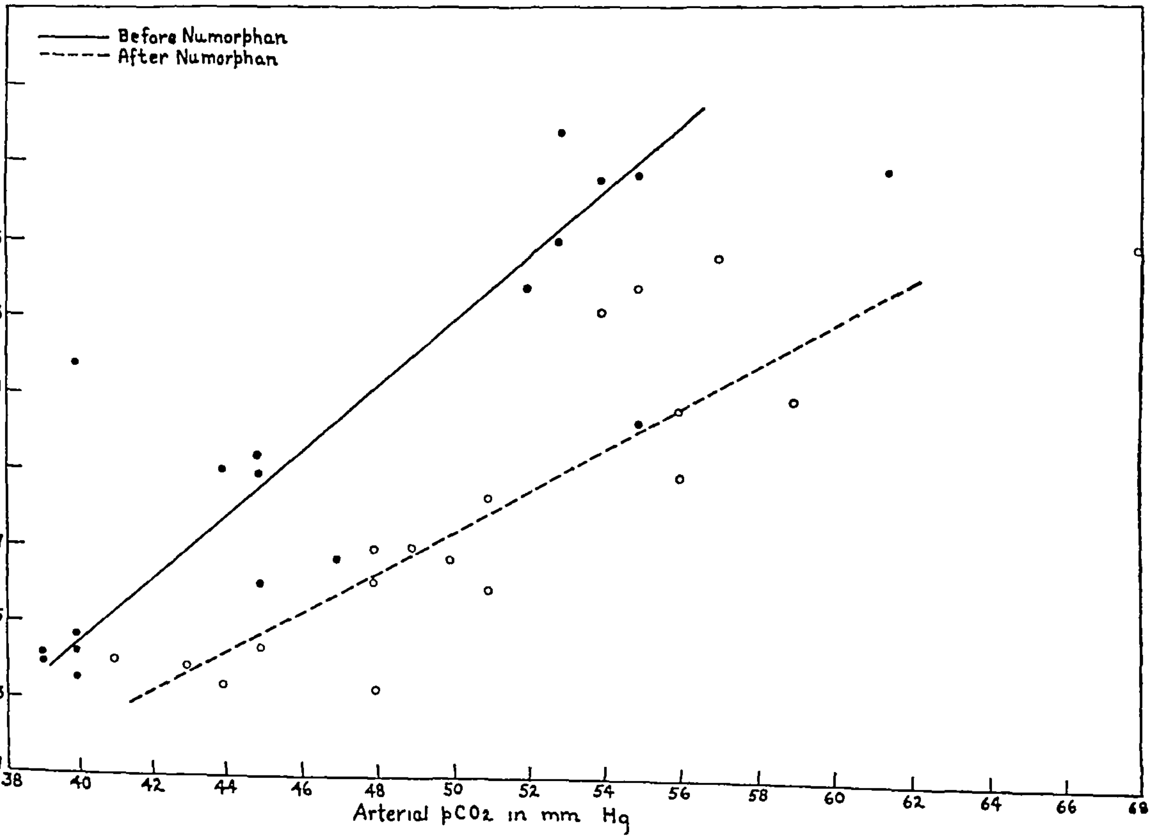

FIG 2 —Composite respiratory response to increased concentrations of carbon dioxide observed in six normal young men before and 40 minutes after subcutaneous administration of 14 hydroxydihydromorphinone (Numorphan)

Results

Definite depression of respiration and a marked reduction in the sensitivity of the respiratory center to carbon dioxide stimulation were observed in all 16 subjects 40 minutes after the subcutaneous administration of a 1 5 mg dose of 14-hydroxydihydromorphinone

In the six normal young subjects breathing compressed air, there was a reduction in the average basal minute ventilation per square meter of body surface area from 4 45 to 4 17 liters, a reduction in arterial pH from 7 41 to 7 37 units, and an increase in arterial carbon dioxide tension from 41 to 45 mm Hg (table 2) Similar changes were observed during inhalation of 4 17 and 5 63% carbon dioxide The arterial oxygen saturation, respiratory rate, carbon dioxide output, oxygen uptake, respiratory quotient, basal metabolic rate, and cardiac output were not significantly changed

The magnitude of the effect of 14-hydroxydihydromorphinone on the respiratory center in the the six normal subjects can be appreciated from the ventilatory response to changes in the arterial carbon dioxide tension (fig 1 and 2) The normal respiratory center is extremely sensitive to small changes in the partial pressure of carbon dioxide in the arterial blood In all six subjects the response was so depressed after the administration of 14-hydroxydihydromorphinone that at any given carbon dioxide tension the volume of minute ventilation was reduced by about 45% The average carbon dioxide tension of this group when they were breathing compressed air increased 4 mm Hg, from 41 to 45 mm Hg The anticipated minute ventilation at this level is 8 6 liters per minute per square meter of body surface area The actual average minute ventilation was 4 17 liters per minute per square meter of body surface area, a 52% reduction below the anticipated level

TABLE 3—*Effect of 1 5 Mg 14-hydroxydihydromorphinone on Ten Patients with Pulmonary, Cardiovascular, or Hepatic Disease*

Disease	Respiratory Rate per Min			Minute Ventilation (l /Min /M^2)			Arterial pO^2 (Mm Hg)			Arterial pH (unit)		
	Before	After	Change %	Before	After	Change %	Before	After	Change %	Before	After	Unit Change
Pulmonary (4 Patients)	17	15	—12	5 37	4 17	—22	43	49	+14	7 41	7 36	—0 05
Cardiovascular (4 Patients)	17	14	—17	4 07	3 46	—15	42	49	+17	7 41	7 36	—0 05
Hepatic (2 Patients)	13	12	— 8	5 12	3 29	—36	35	40	+14	7 41	7 37	—0 04

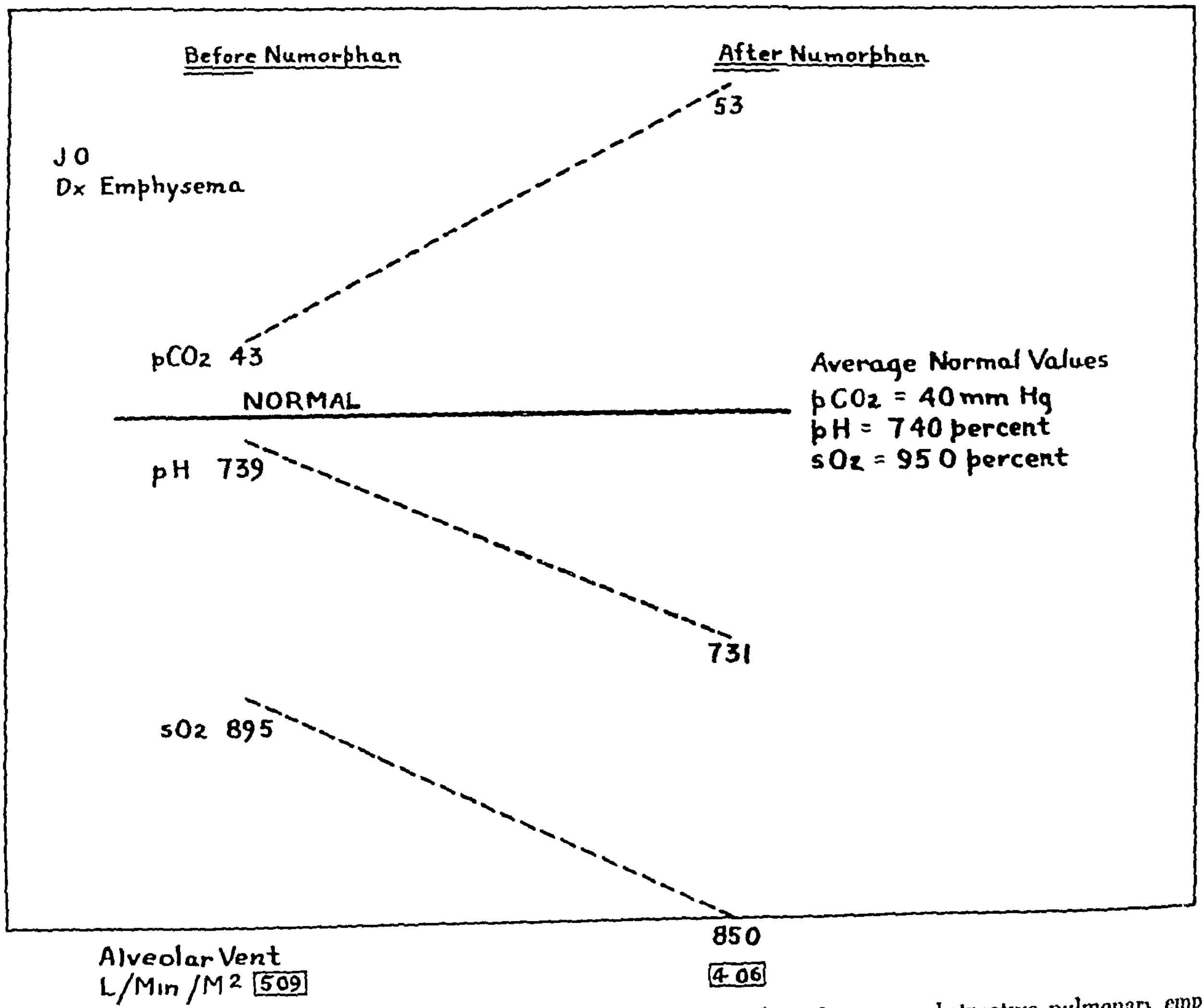

Fig 3 —Respiratory depression produced in 67 year old patient with moderately severe obstructive pulmonary emphysema by administration of 1 5 mg of 14 hydroxydihydromorphinone (Numorphan) Response was typical of that observed in group of older patients with cardiovascular, pulmonary, or hepatic disease

Respiratory depression after the administration of 14-hydroxydihydromorphinone was even more marked in the patients with cardiovascular, pulmonary, and hepatic disease than it was in the normal subjects Periodic breathing resembling Cheyne-Stokes respiration was observed in 5 of the 10 patients in this group after 14-hydroxydihydromorphinone was given One patient with cerebral arteriosclerosis, whose respiratory pattern was already irregular before administration of 14-hydroxydihydromorphinone, developed periods of apne of 30 seconds duration 15 minutes after subcutaneous injection of the drug The respiratory depression was quickly reversed by the intravenous administration of 10 mg of normorphine (Nalline) hydrochloride There was an average reduction in resting minute ventilation for the group of 22%, a decrease in arterial pH of 0 05 units, and an increase in carbon dioxide tension of six mm Hg (table 3)

It is of interest that even in those patients whose minute ventilation was most severely reduced after the administration of 14-hydroxydihydromorphinone there was little reduction in the respiratory rate The reduction in minute ventilation was almost entirely at the expense of the tidal volume, which is very difficult to estimate clinically In 7 of the 10 patients a fall in arterial oxygen saturation was induced by 14-hydroxydihydromorphinone The changes observed in a patient with pulmonary emphysema, who was typical of this group, are shown in figure 3

Comment

The effect of a drug on respiration is occasionally assessed by observing the change induced in the respiratory rate Our observations suggest that the respiratory rate is too gross a measure to be of any value because reduction in rate is a very late manifestation of respiratory depression Minute ventilation, although more accurate than respiratory rate, is also a relatively insensitive measure unless it can be related to changes in the partial pressure of carbon dioxide in the arterial blood In the six normal subjects studied it would have been impossible to evaluate respiratory depression by clinical observation Even the measured change in resting minute ventilation was relatively small after the administration of 14-hydroxydihydromorphinone However, when studies were done which permitted us to relate changes in minute ventilation to changes in arterial carbon dioxide tension, it became apparent that 1 5 mg of 14-hydroxydihydromorphinone had reduced the sensitivity of the respiratory center to carbon dioxide stimulation by about 45%

Although respiratory depression was subclinical in the young, normal subjects, it was usually apparent in the 10 older patients, who had cardiovascular, pulmonary, or hepatic disease The changes in arterial blood gas content were more marked in this group, and periodic respiration was induced in 5 of the 10 patients Examination of our data suggests that clinically significant respiratory depression is not produced in healthy, young subjects by a 1 5 mg dose of 14-hydroxydihydromorphinone However, caution must be exercised with doses of this amount in elderly persons and in patients who are known to be sensitive to central nervous system depressants, such as those with cardiovascular, pulmonary, or hepatic disease

Comparison of our results with data available in the literature on the depressant effect of morphine shows that at comparable dosage levels (1 5 mg of 14-hydroxydihydromorphinone, 15 mg of morphine) the two drugs exert a quantitatively similar depressant effect on the respiratory center[4] Loeschcke and his associates[5] demonstrated an increase in alveolar carbon dioxide tension of 3 mm Hg in young subjects breathing air and a 30% decrease in the ventilatory response to carbon dioxide after the administration of 10 mg of morphine These figures approximate closely our findings of a 4 mm increase in arterial carbon dioxide tension and a 45% decrease in ventilatory response to carbon dioxide in similar subjects who were given 1 5 mg of 14-hydroxydihydromorphinone

Summary

The effect of a new synthetic morphine derivative, 14-hydroxydihydromorphinone (Numorphan), on the respiratory center has been studied in 6 normal, young subjects and 10 patients with cardiovascular, pulmonary, or hepatic disease Respiratory depression was demonstrated in all 16 after the administration of 1 5 mg of the drug The depression was much more marked in the older patients, and Cheyne-Stokes respiration was induced in five

Clinical criteria, particularly the respiratory rate, were found to be insensitive measures of respiratory depression This was most apparent in the younger, normal subjects, in whom respiratory rate remained unchanged and resting minute ventilation was reduced by only 6% in the presence of a 45% reduction in the response of the respiratory center to carbon dioxide stimulation The respiratory depression produced by 14-hydroxydihydromorphinone was equal to that found by others with equivalent doses of morphine

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SPECIAL COMMUNICATION

THE PHARMACEUTICAL INDUSTRY REPORTS

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The pharmaceutical industry's major task is to provide an abundant supply of safe, effective prescription drugs, to discover, screen, develop, and make available new drugs which will decrease or end suffering, to promote longer and happier lives, and to manage to stay in business while it is so doing The following are statements from authorities outside the pharmaceutical industry which illustrate its contributing role

Dr James Watt, director of the National Heart Institute, has said "The major strides in drug discoveries of the past few years have been made within commercial pharmaceutical houses "[1]

Dr Robert H Felix, director of the National Institute of Mental Health, stated "I believe that these (psychotropic) drugs have created more collective enthusiasm and more cooperative endeavor throughout psychiatry and allied sciences than any other single development over the past three or four decades "[2]

The official Hinchcliffe Report of the British Ministry of Health states that "all subsequent antibiotics (after Waksman's discovery of streptomycin on a grant from a drug company) have been discovered by scientists working in the laboratories of pharmaceutical firms, almost all in the U S A "[3]

Since 1947 this industry has spent about one billion dollars in research, which represents perhaps the major risk in the industry The chance that any given research involving a new potential medicine will be successful stands at 2,865 1 against the manufacturer!

Twenty-five years ago the medical profession had only a few drugs capable of striking at the causes of infectious diseases The list of killing and crippling diseases was long In case after case, physicians were forced to prescribe medicines that they knew could, at best, provide only supportive therapy

In the short period of a quarter of a century, disease after disease has been erased from the dread list of cripplers and killers This has been made possible in large part by discoveries and developmental activities of the drug industry—by chemotherapy that today permits a physician to treat many specific organs and to conquer many specific diseases with the precision of a surgeon using a scalpel

What have these plummeting death rates meant? More than 3,000,000 Americans, living today, would be dead if the nation's death rate had remained constant at its 1937 level[4]

At the turn of the century, pneumonia, influenza, tuberculosis, and gastritis accounted for one of every three deaths in the nation The number of recoveries from pneumonia began to rise sharply, simultaneous with development of sulfonamides, and it continued to rise with the introduction of penicillin and other antibiotics Since 1930, death rates due to pneumonia and influenza have dropped 68% The death rate due to gastritis, duodenitis enteritis, and colitis has fallen 82% In the 13 years from 1944 through 1957, the death rate from tuberculosis fell 80% In the same 13-year period, the drop in death rate was 76% for deaths due to meningococcic infection, 78% for deaths due to mastoiditis and ear disease, 74% for deaths due to syphilis, 93% for deaths due to whooping cough, 90% for those due to scarlet fever, and 96% for deaths due to diphtheria

The use of these modern drugs also has cut the incidence of complications for sufferers from infection, made possible surgery that could not be undertaken in earlier years, made people socially more effective, brought unique and special progress in fields such as mental health, and helped to alleviate pain

Every major advance of the United States drug industry has also been accompanied by astronomical dollars-and-cents savings to the American people—from vast reduction in medical expenses made possible by rapid cures for illnesses and the resultant shorter length of hospitalization to the increased productivity of those to whom new drugs have made cure possible

The National Health Education Committee has reported that in just one year the United States Treasury gained more than one billion dollars—and almost six billion dollars was added to the national income—as a result of the decline in mortality rates since 1937 In the field of mental health, the use of psychotropic drugs made possible savings of an estimated 860 million dollars in state mental hospital construction costs in a single three year period by reducing the length of hospitalization required for thousands of patients[5]

President, Pharmaceutical Manufacturers Association Dr Smith was formerly Editor of THE JOURNAL

Reason for Rapid Pace of Discovery

Competition forces each company as a matter of economic survival to dedicate itself to obsoleting its own products Any slackening of competitive research carries with it the prospect of grave decline in future business Competition in research has enabled the United States to lead the world in the output and effectiveness of ethical drugs and has revolutionized not only drug manufacturing but the practice of medicine itself

Last year the drug industry spent almost 200 million dollars in the search for new medicinal agents That is an increase of more than five times the amount it spent for research and development 10 years ago While research plays a major role in the pharmaceutical industry story, other contributing factors also were described to the U S Senate Subcommittee on Anti-Trust and Monopoly in testimony on February 23 and April 20, 1960 (The author will furnish the full text of that testimony, on request, as soon as it is published)

In 1958 the tremendous concentration on research enabled the industry's scientists to test 114,600 substances in laboratories, they searched out new answers to problems including allergy and infectious diseases (50,300 substances tested), arthritis and metabolic diseases (6,300 substances tested), heart disease (8,200 substances tested), cancer (28,000 substances tested), and mental health, neurological diseases, and blindness (12,100 substances tested)

A large part of this research activity was in fundamental investigation or basic research, which the National Science Foundation has defined as research on "projects which are not identified with specific products or process applications, but rather have the primary objective of adding to over-all scientific knowledge In the last year for which figures are available, the drug industry spent between 20% and 25% of its total research budget on fundamental research, in contrast with an all-industry expenditure of about 4% of total research budget for this purpose

In a period of continuing inflation, the wholesale price of drugs consistently since 1948 has resisted upward pressures—rising only 3% in the past 10 years This has occurred at a time when wholesale prices of all industrial products were soaring 22% It has occurred in a period when drug industry costs, such as wages and construction, were spiraling Americans today would be paying one billion dollars a year more for drugs if the price of medicine had gone up only as much in the past few years as the total cost of living[6] The American consumer today, despite all that has been said about drug prices, actually is spending about the same part of his income on drugs as in 1939, before most of our specific high potency drugs were available Drug prices, in fact, have increased only about half as much as fees for doctors and dentists and only one-fourth as much as the rise in hospital rates

The far more effective drugs of 1960 actually take less out of each person's health dollar than did the drugs of 30 years ago In 1930, 20 cents of each American dollar spent for health purposes went for drugs and sundries In 1958 it was 19 9 cents—clear evidence that the price of drugs has not risen relative to the total expenditures for medical care

Prices of new drugs follow a characteristic pattern of decline after introduction and when volume use and production take place By the spring of 1959 antibiotics, vitamins, and steroids were at the lowest price levels in history, their prices had declined precipitously since these drugs were introduced After millions of doses of Salk vaccine were produced by industry in record time, the price of this vaccine was cut to half its original level The initial price of cortisone was $200 per gram, several years later it was $2 per gram The price of penicillin in 1943 was $100 for 100,000 units, in 1946 it was $4 76, by 1956 the price was slightly over 22 cents The price of streptomycin dropped 40% in less than a year Insulin costs 6% of what it did 30 years ago, about the time it was introduced

In most cases in the drug field, the cost of raw materials is relatively slight—similar perhaps to the cost of wheat in a loaf of bread or cotton in a man's shirt The producer's cost must also cover production expenses, selling expenses, research, general and administrative expenses, taxes, licenses, royalties, reserves for depreciation, quality control, and advertising and promotion

In spite of these expenses, the average price of a prescription in the United States today is about $3 More than 60% of all prescriptions cost $3 or less, and only about 1 in 100 prescriptions costs as much as $10 The manufacturer receives about half of the retail cost

Detail Men, Advertising, and Other Educational Media

Detail men form an indispensable link between the doctor and new knowledge that can help or save a patient In a poll of the nation's doctors sponsored by the American Medical Association in 1958, 68% of the physicians interviewed stated that the detail man was the first source of information In a few minutes the detail man can acquaint the doctor with the capacities and the limitations of a new drug

The most important advantage of medical advertising is that it brings new product information to the doctor's attention Any time lag between the approval of a new product and the doctor's knowledge of that product is intolerable where health and often life itself are at stake Advertising, supported by detailing, is the fastest means our free enterprise system has produced to guarantee that the lag between availability of a drug product and its use in treatment is held to a minimum

The ethical drug industry makes many other contributions to medical knowledge in the public interest Such contributions are often and wrongfully categorized as advertising or promotion Educational funds support a large part of most medical society programs through journal advertising and exhibit space They contribute substantially to the economic existence of most medical journals They provide almost all available closed-circuit educational television for physicians They supply a large part of the available medical teaching films They provide for the circulation of reprints, abstracts, and reviews of medical reports printed by medical editors They provide a substantial number of medical seminars each year

These funds also finance millions of samples used by doctors to determine their patients' response to a drug before the patients spend money to fill prescriptions—a vital medical function benefitting both patients and doctors

Brand Names

Fundamental to the successful system of education and distribution is the industry's practice of using brand names rather than generic names of its formulations Like other industries, each member company of the ethical drug industry strives to excel in its products and to make them known so that they will be bought and a coast-to-coast inventory can be maintained The only way for a company to make them known is to give them a name different from its competitor's

Brand name identification is particularly vital for the innovating companies which account for the majority of new drug advances These innovating companies take the initial risk of enormous marketing investments to make their new drugs available—and on the shelves—in the drug stores of the nation, and always with the possibility that the new product may fail through some unforeseen circumstance

By brand name prescription, too, the physician orders for a patient a specific product in which he has absolute knowledge of quality, purity, and any side-effects that might have importance for a particular patient

A system allowing pharmacists to substitute generic equivalents for brand name prescriptions is tantamount to restricting the physician's choice and authority and transferring some of his decisions to the pharmacist Under the American system of medical care, the physician alone arrives at the diagnosis, and he alone should decide precisely what drug is to be prescribed for his patient This is a vital part of the physician's responsibility in medical care, and it is his responsibility alone

Competitive distribution is, in short, a system which insures that the right drug will be available at the right place and at the right time, that it will be prescribed by a physician who knows about it, trusts it, and knows how to use it, and that it will be dispensed by a highly trained, professional pharmacist The most expensive drug in the world is the one that is not available where and when it is desperately needed

1411 K St, N W

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NEW POWERS FOR ACTION—Even when the individual believes that science contributes to the human ends which he has at heart, his belief needs a continual scanning and re-evaluation which is only partly possible For the individual scientist, even the partial appraisal of this liaison between the man and the process requires an imaginative forward glance at history which is difficult, exacting, and only limitedly achievable And if we adhere simply to the creed of the scientist, that an incomplete knowledge of the world and of ourselves is better than no knowledge, we can still by no means always justify the naive assumption that the faster we rush ahead to employ the new powers for action which are opened up to us, the better it will be We must always exert the full strength of our imagination to examine where the full use of our new modalities may lead us —N Wiener, Some Moral and Technical Consequences of Automation, *Science*, May 6, 1960

SPECIAL CONTRIBUTION

CLINICAL USE OF GLYCEROLIZED FROZEN BLOOD

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A practical method now exists for the long term preservation of human blood Red blood cells which have been glycerolized, frozen at —80C, and stored up to 44 months have been deglycerolized, reconstituted, and successfully given to patients Over 1,014 units of frozen glycerolized blood have been administered to patients, with good clinical results and a low reaction rate The Cohn fractionation method permits "tailoring" of the blood to fit the needs of the recipient Frozen heparinized blood has been used as a priming fluid for extracorporeal circulation Frozen plasma retains full heparin activity after storage for five months The stockpiling of blood of rare types and banking by donors for future elective autotransfusions can now be done The stockpiling of blood for use in the event of mass casualties must await engineering changes

Since the discovery of human blood groups by Landsteiner in 1908,[1] there have been only two significant developments in the ability to transfuse human blood These are the use of an anticoagulant to permit the collection of blood at a location remote from the recipient and the development of anticoagulant acid citrate dextrose solution to permit the short-term storage of blood at ordinary refrigerator temperatures Such methods were adequate for transfusion needs of civilian practice until comparatively recent times

With recent progress in medical and surgical skills resulting in the development of heart-lung oxygenators, kidney dialyzers, chemotherapeutic perfusion of isolated cancers, and other procedures requiring large volumes of blood for priming or replacement, the need for blood transfusion has steadily increased At present a shortage of blood of proper type is often the limiting factor in definitive care of the patient In addition, large stockpiles of human blood are also needed to meet civilian and military requirements in case of nuclear attack Many methods of prolonging storage time of human blood have been reported, but none has successfully permitted storage longer than a few weeks[2] Smith and others[3] showed that tissues exposed to glycerol and other polyhydric alcohols could be frozen and thawed without significant damage They suggested that erythrocytes might be preserved in this manner, but the need to remove glycerol from the cells before transfusion prevented its immediate translation to red blood cell preservation Although glycerol is nontoxic, the introduction of glycerolized blood cells into an aqueous solution such as plasma results in excessive swelling and rupture of the glycerolized blood cells because the rate of water endosmosis into the blood cells is four times the rate of glycerol exosmosis The Cohn fractionator was developed in 1951 for the separation of blood into its component parts[4] It possesses certain features uniquely applicable to the glycerolization and deglycerolization of red blood cells The fractionator contains a sterile centrifuge that operates under precise temperature control and has no limitations on the volume of solutions for perfusion of blood cells in the revolving bowl

Preliminary studies by Tullis and his associates[5] have shown that it is possible to use this apparatus for processing of frozen red blood cells Human blood so glycerolized has been stored in the frozen state for periods up to 28 months and, upon subsequent use for transfusion, has had normal in vivo survival[6] In the present report these studies have been extended and the therapeutic effectiveness of the frozen human blood evaluated The equipment and techniques developed for this process have been found to function as satisfactorily at a clinical level as they had under research conditions As a result, a blood bank of frozen human red blood cells has been established[7] These studies were carried out at the United States Naval Hospital, in Chelsea, Mass, under the joint supervision of the Department of the Navy and Protein Foundation of Boston, Mass

Methods

The Blood Research Laboratory and the Military Blood Bank were established at the United States Naval Hospital, in Chelsea, Mass., in June of 1956. The basic equipment, in addition to that routinely used in any research laboratory, included a Cohn (ADL) fractionator with individual insert bowl units (cartridges), freezing facilities capable of maintaining −80 C and −120 C temperatures and a special autoclave for sterilization of the cartridges with their attached disposable bags. The laboratory personnel comprised six persons: two professional supervisors, one technician, one laboratory helper for washing cartridges and sterilizing solutions, and two persons without prior technical experience who were trained in the operation of the centrifuge and the assembly of the cartridges and their attached bags.

All blood from donors was drawn in a phlebotomy room at the laboratory. The donors were active duty military personnel who met the standard blood bank criteria for blood donation. Approximately 475 cc of blood was collected into 75 cc of acid citrate dextrose anticoagulant solution (NIH Formula A) in a plastic bag. The bag of blood was then connected to a sterile cartridge with attached glycerol solutions and placed in the fractionator. Details of the operation of the centrifuge have been separately reported.[8] The only important changes in glycerolizing technique were modifications of the composition of the washing solutions and resuspension media to that noted in table 1. The presence of ionic magnesium in the washing solution appeared to improve slightly the rate and effectiveness of the glycerol exchange. The concentrations are shown in table 1, but, subsequent to the present study, the magnesium concentrations have been reduced to 0.004M in all glycerolizing and deglycerolizing solutions. The minimum time elapse for glycerolization and deglycerolization has been reduced to 35 minutes and 45 minutes respectively.

The blood was usually processed for frozen storage on the day it was collected, but acid citrate dextrose-treated (A C D) blood held for three days before processing resulted in minimal difference in the ultimate recovery rate of the cells. These data suggest A C D blood may be held longer than three days before processing for frozen storage. When platelets were desired, the plasma from the original red blood cell separation was run through the fractionator using a platelet bowl[9] and stored in gelatin at 4 C. When desired, the platelet-free plasma was then coupled in tandem with the glycerolized cells and placed directly into low-temperature-freeze lockers. At a glycerol concentration between 40% and 50%, it was unnecessary to have rapid freezing or control of the freezing rate. Thermopile readings from within the red blood cell mass indicated that the blood reached ambient temperature of the locker in about eight hours. Three deep freeze lockers were available, each with an average capacity of 150 pints. Two of the lockers were maintained at a −80 C, and one at a −120 C.

Auxiliary generators were available in case of power failure, but no serious breakdown of equipment or power occurred in the three years the laboratory has been in operation. Despite these precautions, there is no evidence that accurate control of temperature is critical during storage, experiments now in progress suggest that transient thawing and refreezing does not significantly alter the final blood

TABLE 1.—Composition of Glycerolizing and Deglycerolizing Solutions and Resuspension Media

		Final Concentration
Glycerolizing Solutions		
Wash solution #1, 300 ml. per unit of red blood cells*†	Glycerol 1000 Gm. Sodium lactate 89.6 Gm. Dextrose 10 Gm.‡ Potassium Chloride 1.5 Gm. Magnesium Chloride 4 Gm. Distilled water q. s. 5 liters	20% w/v 0.16 M 0.2% 0.004 M 0.008 M
Wash solution #2, 1000 ml. per unit of red blood cells*	Glycerol 10,000 Gm. Sodium lactate 350.4 Gm. Dextrose 40 Gm.‡ Potassium Chloride 5.96 Gm. Magnesium Chloride 32.5 Gm. Distilled water q. s. 20 liters	50% w/v 0.16 M 0.2% 0.004 M 0.017 M
Deglycerolizing Solutions		
Wash solution #1, 1500 ml. per unit of red blood cells*	Glycerol 200 Gm. Sodium lactate 1112.4 Gm. Dextrose 20 Gm.‡ Potassium Chloride 5.96 Gm. Magnesium Chloride 32.5 Gm. Distilled water q. s. 20 liters	10% w/v 0.5 M 0.1% 0.004 M 0.017 M
Wash solution #2, 1500 ml. per unit of red blood cells*	Sodium lactate 350.4 Gm. Dextrose 20 Gm.‡ Potassium Chloride 5.96 Gm. Magnesium Chloride 16.2 Gm. Distilled water q. s. 20 liters	0.16 M 0.1% 0.004 M 0.008 M
Wash solution #3, 600 ml. per unit of red blood cells*	Sodium Chloride 180 Gm. Dextrose 20 Gm.‡ Distilled water q. s. 20 liters	0.15 M 0.1%
Resuspension Medium § ¶		
	Albumin 25% 2400 ml. Sodium Chloride 83.5 Gm. Dextrose 48.0 Gm.‡ Potassium Phosphate monobasic 10.44 Gm. Distilled water q. s. 12 liters	5% 0.12 M 0.4% 0.0025 M

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*All solutions adjusted to pH 7.

†One unit of red blood cells is defined as the red cell mass obtained from 475 ml. of blood collected in 67.5 ml. of ACD anticoagulant solution.

‡For sterile solutions use the equivalent amount of dextrose after sterilization in the form of a sterile 5% dextrose solution.

§For packed red cells use 60 ml. per unit of red blood cells. For whole blood replacement use 250 ml. per unit of red blood cells.

¶For reconstituted "Whole Blood" use 200 ml. of original plasma per unit of red blood cells.

cell yield or survival Coded chart racks were used to indicate the contents in terms of blood groups and date of storage Removal of units from storage was based on blood bank needs and upon a plan established for this study to use, for transfusion purposes, an adequate number of blood specimens stored for one day to four years

After removal from the deep freeze, the individual bags containing blood were thawed by immersion in a rotator water bath at 37 C for ten minutes These bags were then attached by sterile plastic adapters to the same centrifuge bowls used for the original glycerolization, except for modification of the plastic assembly to provide for deglycerolizing solutions The thawed blood cells flowed into the centrifuge bowl (by gravity), after which, wash solutions were introduced in a manner similar to that of the glycerol incorporation The processed blood cells were finally resuspended in one of three solutions, depending on clinical requirements, (1) 60 ml of 5% albumin media for "packed" red blood cells, (2) 250 ml of 5% albumin media for blood volume replacement, or (3) 200 ml of the plasma from the same blood for reconstituted "whole" blood After completion of processing, the reconstituted blood was kept under standard refrigeration for up to 10 days if resuspended in the 5% albumin media or up to 14 days if resuspended in its native plasma

Bacteriologic control on the process was maintained by culturing three blood agar plates, three Sabouraud's slant tubes, and three thioglycolate tubes, and one of each culture was held at temperatures of 32 C, 23C and 4C for each unit processed In addition, a Gram stain was obtained from the contents of an isolated pilot tube on each bag of reconstituted blood, prior to transfusion After 2,000 consecutive operations of glycerolization and deglycerolization, no bacteriologic contamination from the processing was found Accordingly, the practice of nine independent cultures per blood unit was reduced to three cultures per unit, followed by a Gram stain at the time of final cross-match

Routine checks of supernatant hemoglobins were also made In the beginning of the study, these were often found as high as 0 5 gram After correction of an abnormally low pH found occasionally to be present in the commercial lactate solution marketed with pH indicated as 7 0 and with subsequent careful regulation of the pH of the washing solutions, free hemoglobin present after red blood cell processing was sharply reduced to a current range of 35 mg % to 200 mg %

At the present time, by using two Cohn fractionators, it has been possible, on an eight-hour day, five-day week basis, to operate at a level of 400 glycerolizations or deglycerolizations per month

Results

Operational Capacity—This report covers data obtained at the United States Naval Hospital, Chelsea, Mass, during the period from September, 1956 through January, 1960 inclusive, plus unreported data on blood cells preserved at The Protein Foundation between 1955 and 1956 and removed from storage and used for transfusion purposes at the United States Naval Hospital, Chelsea, Mass, or the New England Deaconess Hospital, Boston, in 1959 as a part of the same experimental project Since the inception of the project, 37% of the blood administered at this Naval Hospital is supplied from the freezer lockers of the Blood Research Laboratory Between August, 1956 and January, 1960, 2,012 units of blood were collected, separated into plasma and cells in the Cohn (ADL) fractionator, and glycerolized and frozen Of these operations 97% were without technical failure The present monthly rate of loss through breakdowns in collection, separation, and glycerolization is less than 1% 1,323 units were stored at a temperature of —80 C, and 617 units were stored at a temperature of —120 C These glycerolized units of blood were subsequently removed from storage and processed for experimental study or for transfusion

Only 23 units of blood were damaged in storage or lost during thawing Of the 1,471 units of blood deglycerolized, all but 220 were suitable for transfusion These 220 units represented loss from all causes, including broken bags, low yield, personnel error, equipment breakdown, autoclave breakdown, defective water supply, resuspension media contamination, and high supernatant hemoglobin Each of these variables was corrected with a minimum of effort or time lost from routine operation in preparation of blood for use in the Blood Bank at this hospital Most of the losses occurred early in the study During the last three months preceding this report, a total of 289 units of blood were deglycerolized in the laboratory, with a loss of three units (less than 1%)

With increasing confidence in the safety and therapeutic effectiveness of the blood, the rate of clinical use has increased until in March, 1959, this blood became standard issue for blood transfusions at this hospital The collection of rare types of blood, a normal outgrowth of this procedure, has increased, some patients with rare types of blood have deposited their own blood in anticipation of elective usage

Red Blood Cell Viability—The in vivo survival of 14 units of deglycerolized erythrocytes in storage from 1 to 44 months was determined by the Cr^{51}-tagging method After tagging, 70 to 350 milliliters of each unit were infused into healthy volunteer recipients, and the survival of the tagged erythrocytes measured at one-to-four-day intervals for the next two months Three units were studied in patients whose illnesses were not expected to shorten red blood cell survival, and four units were administered to patients with hemolytic anemia, hemorrhage, or malignancy Two units of A C D blood were tagged with radio-chromate and administered to normal recipients for comparison purposes

The results obtained are summarized in table 2 The 24-hour survival of the deglycerolized erythrocytes ranged from 84 to 96%, with a mean of 90% in the normal recipients The half-time survival ranged from 19 to 34 days, with a mean of 30 days in this group, independent of the time of storage The results of half-time survival studies in the seriously ill patients were what could be expected and compared with the reported studies using A C D blood For an additional 32 units of deglycerolized blood 3 days to 43 months, the survival of deglycerolized cells 24 hours after administration to seriously ill patients was determined by a similar Cr^{51}-tagging technique The 24-hour survival rate of these blood cells ranged from 68 to 98%, depending on the patient's illness, and was again independent of storage time

TABLE 2.—In Vivo Survival of Cr^{51} Tagged ACD and Deglycerolized Erythrocytes

Treated Blood, Duration of Storage	24 Hour Survival, %	Half Time Survival, Days, No
ACD—2 Days	97	36
ACD—20 Days	87	32
[2]Deglycerolized—1 Month	86	30
Deglycerolized—4 Months	96	32
[2]Deglycerolized—4 Months	84	30
[1]Deglycerolized—9 Months	94	25
Deglycerolized—13 Months	84	32
Deglycerolized—16 Months	89	32
Deglycerolized—18 Months	91	34
[2]Deglycerolized—23 Months	90	19
Deglycerolized—36 Months	95	30
Deglycerolized—44 Months	94	35
[3]Deglycerolized—2 Months	80	9
[3]Deglycerolized—5 Months	90	15
[3]Deglycerolized—10 Months	90	21
[3]Deglycerolized—21 Months	81	18

[1] Unit held at 4C for 72 hours before glycerolization and freezing
[2] Used in hospitalized patient with expected normal survival
[3] Used in hospitalized patient with expected short survival

It would appear from these studies and others in progress that these blood cells kept in a frozen or ametabolic state for as long as 44 months have almost normal behavior and survival Other chromium studies indicate that an average of 82% of the original cells taken from the donor actually reach the vein of the recipient Most of red blood cell loss of 18% is due to mechanical rather than hemolytic loss and appears to be independent of the storage time factor This loss can be significantly reduced by current design modifications of the mechanical equipment

Clinical Observation.—The clinical aspects of this study began in July of 1957 when the first unit of packed red blood cells was given at the Chelsea Naval Hospital Selected cases needing red blood cell replacement only were studied, and these blood cells were found to be adequate for this purpose However, it soon became evident that there was an equally great need for blood for volume replacement during surgery or in cases of trauma Originally only the red blood cells had been stored, the plasma having been fractionated into its component parts Before the blood cells could be used for transfusion in surgery, a suitable volume expander had to be added The packed blood cells in their 60 cc albumin solution had hematocrits up to 65%, and, therefore, could be further diluted and still have a hematocrit of normal blood Inasmuch as the standard for most volume expanders is a comparison with 5% albumin, it was decided to dilute the units of packed red blood cells with 5% albumin to approximately 500 cc This could be accomplished without modification of the process

Units of frozen red blood cells, resuspended to a volume of 500 cc with 5% albumin, were first used for supportive therapy of preoperative and postoperative patients in the intensive therapy ward, where they were studied and observed by trained personnel This blood was found to be quite satisfactory from both a clinical and a laboratory point of view as a volume expander in the treatment of shock It was next used as measured volume replacement during surgical procedures In evaluating the efficacy of this blood, in addition to standard clinical observations, pretransfusion and post-transfusion hemograms and urinalyses were obtained In 25 patients where it was anticipated that large volume replacement would be necessary during surgery, preoperative platelet counts, serum bilirubins and urinary hemoglobins were obtained In 10 patients blood volume determinations by the tagged chromium method were made These studies were repeated immediately before the operation, on the first postoperative day, and again one week postoperatively

Table 3 shows the results in 10 patients who received massive measured blood replacement in the operating room and the number of units that each received Estimation of the blood loss was based on weight of sponges, drapes, and suction bottles As can be seen, the blood cell mass held up well in all of these patients as did their circulating blood volume The other hemogram studies remained within the range of normal

These laboratory findings have confirmed a clinical impression, that in all patients in whom the blood was used for volume replacement, red blood cells resuspended in the 5% albumin menstruum were adequate There has been no clinical difference observed in the efficacy of the blood, whether resuspended in the 5% albumin menstruum or in its own plasma During the period from July, 1957 to January, 1960, a total of 1,014 units of blood were given These are in addition to the units administered solely for red blood cell survival study Up to the last six months, all of these units were given in serum albumin Since that time 154 units have been resuspended in their own plasma, which had been preserved at —80 C Of the 1,014 units used in transfusions, 446 units had been stored 3 months or less, 414 units had been stored from 3 to 6 months and 154 units had been stored from 6 months to 44 months No relation was observed between the time of storage and clinical effectiveness Eight hundred and ninety eight of these units were given at the Chelsea Naval Hospital to a total of 355 patients Two hundred ninety patients received three units or less, 65 patients received four or more transfusions, and 5 of these received as many as 16 units during a single surgical procedure No abnormal bleeding tendency has been noted in any of these patients receiving massive transfusions of red blood cells resuspended in 5% albumin solution despite the absence of coagulation factors The prothrombin times, fibrinogen levels, platelet counts, coagulation and bleeding times approximated preoperative levels

Reaction Rate—A gratifying feature of the frozen red blood cell program has been the exceptionally low reaction rate in recipient patients In the 1,014 transfusions given to date, there have been only four nonspecific reactions Two of the patients developed urticaria following administration of a unit of blood resuspended in serum albumin solution processed from previously outdated material Two other patients developed mild chills and transitory fevers up to 102 F (38 8 C) One of the latter patients who had an acute leukemia with a pyogenic infection, was having frequent chills and fever However, because one episode of chills occurred during the transfusion, he is included in this series

TABLE 3 —Blood Volume Studies Evaluating Replacement During Surgery

		Immediately Preoperative			First Postoperative Day		One Week Postoperative	
Patient	Type of Operation	RBC* Volume, cc	Plasma Volume cc	Blood Given for Measured Replacement cc	RBC* Volume cc	Plasma Volume cc	RBC* Volume cc	Plasma Volume, cc
1	Gastrectomy subtotal	1490	1980	1300	1580	1790	1500	2100
2	Transthoracic hiatal hernioplasty	1990	2160	892	1850	1770	1900	2700
3	Pleurectomy apical right	2080	2550	1415	1920	1780	2140	1690
4	Splanchnicectomy transthoracic	1760	2630	809	1830	2520	1600	2600
5	Thyroidectomy and radical neck dissection	1422	2046	1920	1440	1800	1390	2280
6	Thoracotomy wedge resection	1840	1920	825	1870	1660	2150	1680
7	Radical hysterectomy (Wertheim procedure)	1210	1420	2485	1540	1730	1400	2100
8	Gastrectomy subtotal	1620	1980	1770	1410	1410	1550	1500
9	Gastrectomy subtotal	2465	3260	2320	2415	2835	2310	3940
10	Esophagectomy	2125	1775	2294	1700	1500	1420	1730

* RBC=Red blood cell

After administration of 500 units of frozen red blood cells resuspended in heated albumin, it was observed that no case of homologous serum jaundice had occurred, although this disease is endemic among our donor population This number of units was too few for the results to be significant, but it seemed possible that the plasma separation or glycerol incorporation had washed out or had inactivated the hepatitis virus For this reason, as well as the clinical needs noted above, 154 of the more recently acquired units of blood have been resuspended in their own native plasma which had been separately stored in a tandem bag These units were used as a control group to determine the possible freedom of the cells from virus One case of homologous serum jaundice has already occurred in a patient who received two such control units This study will be continued with interest

The over-all incidence of reactions therefore is less than 0 5% which is 10 times less than the general reaction rate for standard A C D blood This includes all types of reaction, pyrogenic, urticaria, hemolytic, and even the hepatitis case which occurred in the control Patients with chronic illnesses such as aplastic anemia and chronic leukemia, who require repeated transfusions, frequently develop reactions to all transfusions It is interesting to note that patients who previously had been unable to receive transfusions without having reactions were able to receive this blood without any reaction whatsoever One patient in our series at the Naval Hospital has received a total of 28 units of blood over a period of two years, with adequate replacement and no reactions

Use of Frozen Blood in Extracorporeal Circulation—Recent studies have demonstrated the effectiveness of this blood as a prime' for pump-oxygenator use in open-heart surgery and in isolated cancer perfusions Blood was processed by the routine method as outlined except that it was originally collected in heparin rather than A C D solution The heparinized plasma was stored in tandem bags with the glycerolized frozen red blood cells at a temperature of —80 C After storage for up to five months, the cells were deglycerolized and resuspended in their own plasma Full heparin activity remained Blood so processed has been circulated for three hours at 32 to 37 C in a pump oxygenator In three such experiments (each requiring a prime of 3,000 cc of blood), the loss of red blood cells, as measured by Cr^{51}-labelling was 15 ml, 10 7 ml, and 15 ml respectively This constitutes an average loss of 0 45% The supernatant hemoglobin liberated by the trauma of the pump during the first 120 minutes was less in the one instance than in a control study using six units of A C D blood On two occasions six units of heparinized, frozen, reconstituted blood have been used in vivo during surgery requiring extracorporeal circulation, with similar satisfactory results This "heparin work" has been under the supervision of Lieutenant Thomas G O'Brien, M C, U S N R, and it will be reported in detail separately

Operational Costs —No attempts were made to operate this study on a close, cost-accounting basis Yet, despite the nature of the study and the research design of the basic equipment, a recent survey has shown a surprisingly favorable cost estimate The total cost of disposable bags, tubing, solutions, and labor involved in processing, storage, reconstitution, and final preparation was $14 10 per unit of blood If the basic equipment costs were added with amortization over a five-year period at an operational level of 3,000 units per year, the over-all unique cost, exclusive of overhead for heat and buildings, was $16 40 per unit With minor engineering study and development of a "production" type of Cohn fractionator (stripped of its research attachments) and use of commercially prepared solutions and disposable cartridges, it is estimated that a significant further reduction in cost could be achieved

Comment

A study was undertaken to ascertain concerning the glycerolization and deglycerolization techniques of Tullis and his associates[5] (1) whether it would be safe, reliable, and practical under the operating conditions of a standard hospital blood bank and be sufficiently simple as to be capable of operation by nonprofessional personnel, (2) whether the red blood cells so processed and stored would be consistently sterile, pyrogen-free, and nontoxic, and (3) whether the red blood cells so processed would show normal functional characteristics in vivo and have a life span equivalent to standard banked blood stored at temperatures above freezing

The results reported justify a positive answer to each of these questions, and a practical method now exists for the long-term preservation of human blood The final dating period for such preservation remains to be established, but the in vivo survival studies indicate that the in vivo span of processed red blood cells is normal after storage for the four years covered by this study It remains to be determined whether the yield of transfusible blood cells after four years of storage will be high enough to justify such prolonged storage Data are now available showing that the yields are adequate and unrelated to storage time for at least two years The logistics of blood banking can now be changed, if desired, from the present limitation of 21 days of storage to 24 months or more The immediate reduction in wastage of blood through outdating and a simultaneous assurance of adequate supplies of rare types of blood, without resort to appeals for emergency donors, can also be assured The effect of such long-term storage of human blood on the medical management of mass casualties will have to await the installation of sufficient equipment to simultaneously process many units of thawed, glycerolized blood However, even the existing equipment and stores of blood now on hand in this laboratory could make a major contribution to the medical management of casualties in a minor catastrophe

Even under nonemergency conditions, the glycerol-freezing method possesses unique features sufficient to justify its widespread use The washing method of removing the glycerol simultaneously removes leukocytes, platelets, and products of dead cells This may be the reason for the high clinical tolerance of this blood and a recipient reaction rate tenfold less than the general average

Clinical experience has demonstrated the effectiveness of these red blood cells resuspended in 5% serum albumin solution rather than their own plasma Not only is the danger of serum hepatitis probably reduced, but the plasma is then available for fractionation into its valuable components Using the 5% serum albumin solution as the basic resuspension media, the various components can then be added or subtracted to fit the needs of the patient As an example, it is now possible to produce blood at a selected pH range, and the clinician can order blood of appropriate pH for a patient with an acid-base disturbance Frozen red blood cells in serum albumin solution contain no clotting elements and have been found to be suitable for transfusion in all types of vascular surgery Clotting elements, platelets, and globulin fractions are available and can be added as indicated Blood with extremely low potassium levels (less than 1 mEq/liter) has been used for patients with uremia or renal shutdown who need blood replacement

Cell-function studies on the stored, deglycerolized cells are now in process at the laboratory of the United States Naval Hospital, Chelsea, Mass, to determine the changes if any, that occur in the cell structure during this procedure and to determine how these cells function in gas exchange These studies will be the subject of reports to be published later Preliminary in vitro data and the clinical observations indicate that these blood cells function in a normal manner The studies on stored, heparinized blood may be of singular significance in elimination of the present bottleneck of inadequate supply for cardiothoracic surgery Preliminary studies with the same apparatus used in the blood preservation suggest it may be modified as a simple no-prime oxygenator or dialyzer

Conclusions

It is possible to establish and operate a bank of frozen red blood cells in a hospital at a practical level The Cohn (ADL) Fractionator is a reliable machine for applying the "glycerol-freezing' technique to long-term red blood cell preservation Moreover, it has been shown that this equipment can be operated by personnel who have not had previous scientific, technical, or medical training and at an acceptable operating cost Blood which is collected, processed, frozen for a period of time up to 44 months, stored, thawed, reprocessed, resuspended in plasma, and stored for an additional period at 4 C has in vivo survival and functional characteristics comparable to freshly drawn A C D-treated blood Blood processed in this manner has a final yield of red blood cells which averages 82% after at least two years in storage Red blood cells so handled produce a lower incidence of reaction of all kinds when used for transfusion than whole blood collected and stored by conventional methods

The following persons have contributed to the success of this project Robert B Pennell, M D, Protein Foundation Boston, Leo Olner, M D, Veterans Administration Hospital Indianapolis, Achot Khoubesserian, M D, Cambridge, Mass Lieut John A Cavins, M C, U S N R Lieut Thomas G O Brien, M C, U S N R, Theodore G Drugas M D, Chicago, Lieut John Zemp j g M S C, U S N R and Elton Watkins Jr, M D Lahey Clinic Boston

The opinions or assertions contained herein are those of the authors and not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large

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THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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CONTINUING MEDICAL EDUCATION

A PART of the traditional ethic of the medical profession is that each physician should continue to learn throughout his professional career. An apt statement of this occurs in a part of the Oath and Prayer of Maimonides, a physician of the 12th century, as follows: "Grant me strength, time and opportunity to correct what I have acquired, always to extend its domain, for knowledge is immense and the spirit of man can extend infinitely to enrich itself daily with new requirements. Today he can discover his errors of yesterday and tomorrow he may obtain a new light on what he thinks himself sure of today. Oh God, Thou hast appointed me to watch over the life and death of Thy creatures, here I am ready for my vocation."

Section 2 of the Principles of Medical Ethics of the American Medical Association restates this tradition, somewhat more succinctly, as follows: "Physicians should strive continually to improve medical knowledge and skill, and should make available to their patients and colleagues the benefits of their professional attainments." In perfecting this statement, the Association interpreted it to mean that physicians are ethically bound to improve their own medical knowledge and to contribute new knowledge to medicine.

In its effort to be of assistance to members of the medical profession in their continuing medical education, the Council on Medical Education and Hospitals presents its sixth annual list, Postgraduate Courses for Physicians, in this issue of THE JOURNAL, p 1669, for the year beginning September 1, 1960. Unlike the lists of medical schools, internships, and residencies published by the Council—which include only approved programs—the information on postgraduate courses does not carry either approval or disapproval by the Council of the programs listed, and such should not be inferred by the reader.

It is possible that excellent educational opportunities are not listed, simply because information about them was not available at the time the list was prepared. However, during each of the past two years, more than 90% of the courses which ultimately came to the attention of the Council were included in the annual list. It is also possible that some of the courses listed do not offer the quality of educational opportunity that could be desired. It is hoped that a satisfactory appraisal mechanism of continuing medical education courses can be implemented by the Council, in order that, in the future, a recommendatory list of courses can be published as a greater service for the medical profession.

THE RED WOLF DISEASE

Systemic lupus erythematosus (SLE as favored by the alphabet addicts, with whom I am in sympathy[1]) no longer is an oddity in clinical medicine. The apogee is not to feel secure in having recognized an example or two in clinical practice. Rather the race today is to suspect the malady at the earliest possible moment on the basis of one or more of a significant number of findings and, thereby, to inhibit the inevitable development of grave regressive changes. Systemic lupus erythematosus derives its name from the ravishing character of the morbid process in the late clinical stages (L *lupus* wolf). The butterfly rash on the malar prominences (erythematosus) likewise may be a late manifestation. Frequently the disease runs the entire clinical course without this particular characteristic component.

The alterations that appear early in the disease, the first detectable feature of a morbid reaction, are commanding attention at the present time. Dameshek,[2] in a review of the immunologic observations which are accumulating rapidly, places lupus clearly in the category of an autoimmunologic malady. One of the first clues to this concept was the observation that patients with lupus frequently displayed a false positive serologic reaction for syphilis. Furthermore, a few patients who carried a false positive serologic test, known only to the patient and the physician, with a negative treponemal immobilization test and without other evidence of systemic disease, at some later time have developed clinical symptoms highly suggestive of SLE. The presenting symptoms in other patients with lupus have included an autoimmune hemolytic anemia, idiopathic thrombocytopenic purpura, or evidence of prothrombin and thromboplastin inhibitors in the blood.

Each of these findings is identified with ominous immunologic abnormalities. The effect of one or more of these autoimmune disturbances upon the blood vessels presumably would lead eventually to the full-blown clinical picture. If the insult were mild and localized to a noncritical structure such as the spleen, the disease might not disclose its true malignant characteristics. If several systems were affected, especially the kidneys and the heart, its identity could not long remain unrevealed Thus, some patients with lupus most surely have been victimized by an autoimmune process for years before suspicion progressed to revelation Evidence of critical involvement of cardiac or renal failure in other patients led no critical clinician astray

Dameshek poses the question of origin of the autoimmune chain of events A virus or a chemical may provoke the potential lupus patient to manufacture foreign or abnormal antibody-producing cells, which later elaborate one or more antibodies When the process is multiple, several immunologic disturbances appear Evidence in support of an autoimmune mechanism seems convincing for systemic lupus erythematosus These revelations may be but the beginning of a new era in the definition of the etiology of previously undetermined clinical entities One need not search far to recount other probabilities Rheumatoid arthritis may be such a malady Witebsky[3] reported convincing evidence several years ago for the autoimmune etiology of thyroiditis Addison's disease and chronic pancreatitis are other intriguing possibilites If the red wolf disease points the way, other maladies may follow in its wake

J H T

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1 Talbott J H and Ferrandis R Collagen Diseases New York Grune & Stratton Inc 1956

2 Dameshek W What Is Systemic Lupus? editorial Arch Int Med **206** 162 (Aug) 1960

3 Witebsky E and others Chronic Thyroiditis and Autoimmunization J A M A **164** 1439 1447 (July 27) 1957

IF THE CAT SCRATCHES

A new clinical entity characterized by subacute lymphadenitis, in which the lesion frequently suppurated and healed without a scar was reported in 1950 by Debre and his co-workers The patients often had a history of being scratched by a cat As pointed out in an editorial,[1] while Foshay of Cincinnati was studying tularemia, he recognized the same entity, which was 20 years before the French workers described it He prepared an antigen from the pus of an involved lymph node that gave positive reaction on intradermal injections Foshay did not report these observations, however, he had given Debre a supply of his antigen In 1889, Parinaud presented a report before the Ophthalmologic Society of Paris involving three cases of conjunctivitis, acquired from slaughterhouse animals, in which the regional lymph nodes were enlarged Allen defined Parinaud's oculoglandular syndrome as a conjunctivitis with a definite clinical picture

Debre found that his patients had a positive intradermal reaction to an antigen prepared by Foshay Mollaret and his collaborators announced the discovery of the particular virus causing the disease This was not confirmed by other workers Daniels and MacMurray, in 1954, presented an analysis of 160 cases of cat scratch disease, of which 27 were studied by them and the rest were reported by physicians who proved their diagnosis by intradermal reaction to one of their antigens These cases occurred in 27 states and 8 foreign countries Spaulding and Hennessy[2] of Toronto report their findings in 83 cases, 46 of which were observed personally They define the cat scratch disease as a subacute granulomatous lymphadenitis, which is sterile when tested for the isolation of fungi, bacteria, or viruses At the present, the only more or less specific test is a positive reaction of the skin test The patients reported by them had lymphadenitis and a positive reaction to the skin test

Attempts to isolate an organism have failed Bacteriological and mycological tests, egg yolk inoculation, mouse brain inoculation, and subcutaneous and intraperitoneal injections in guinea pigs have proved negative Tissue culture passages have been made in a variety of cells including HeLa, human conjunctival epithelium, monkey kidney and lymph node, adult cat kidney, human embryonic liver, and peripheral blood cells, with no evidence of cytopathogenic effect

The role of cats in the transmission of the disease is well established Although most of the cats concerned in the Canadian series remained healthy five were sick about the time the patients became ill, and two of the five cats died, one with a diagnosis of enteritis Spaulding and Hennessy emphasize the seasonal incidence in their series, at least in Canada The disease was most prevalent during the winter months from October to January Most of their patients gave a history of contact with a cat, and about one-half of the patients gave a history of an actual scratch The incubation period from the time of scratch until the onset of adenitis varied from 7 to 61 days, usually being 7 to 14 days Adenitis was observed in all areas of superficial lymph nodes of the body Axillary and cervical areas were most often involved The nodes were usually tender and occasionally enlarged to 8 to 10 cm in diameter The adenitis progressed to suppuration in 26 of their 83 cases

The disease usually ran a mild course, with fever, malaise, anorexia, and fatigue Occasionally there were noted pain near joints, phlebitis, paronychias erythema *nodosum*, multiple sites for adenopathy, splenomegaly, and encephalitis, which was rare occurring in one patient only The leukocyte count of the blood was usually normal or slightly elevated The erythrocyte sedimentation rate was often moderately elevated

The skin test was of considerable help in diagnosis The antigen for this test was prepared from the purulent material of patients known to have cat scratch disease The pus is diluted, one part in four parts of physiological salt solution and heated for two hours at 60 C one day and for one hour at

60 C on the succeeding day A positive reaction to the skin test consists of an area of induration at least 5 mm and of erythema of at least 10 mm in diameter 48 hours after the intradermal injection of 0 1 ml of material The skin test becomes positive soon after the onset of the illness The lymphogranuloma venereum complement fixation test is of some diagnostic importance, in dilutions of not less than 1 8 Cat scratch disease may simulate many lymph node lesions such as tularemia, infectious mononucleosis, lymphosarcoma, Hodgkin's disease, tuberculous adenitis, lymphogranuloma venereum, and benign or malignant tumors of the lymph nodes

There is no specific treatment for this clinical entity Neither sulfonamides nor antibiotics have an effect upon its course If the nodes suppurated, aspiration—repeated if necessary—was effective in nearly all cases

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THE GOLD-HEADED CANE

The hallmark of the carriage trade of medical practice in England in the 18th century was the gold-headed cane The story of the ascendancy through five generations of practitioners of one eminent cane is recounted, with many asides, by a supposedly anonymous editor speaking for the cane My copy of "The Gold-Headed Cane" is a second edition published in 1828, presumably with no editor [1] The boards probably are original, less than one square inch of the back strip was salvaged by the book binder who refurbished the monograph in its present state The salvaged scrap includes a portion of the title A zinc etching of the botanical gardens of Chelsea is reproduced on the flyleaf The 1864 edition edited by William Munk was published by Longmans, Green and Co A reprinting of the volume in 1915 carries a foreword by William Osler and a title page, with William MacMichael as the editor The widow of Matthew Baillie, the last of the five wearers of the cane, presented the venerated walking stick to the new College of Physicians of London in 1825 The coat of arms of each of the celebrated physicians is engraved on the gold head of the cane, which rests among the relics of that learned body

The history of the stick is a void prior to 1689 The tale begins with Dr John Radcliffe, physician to Queen Anne and King William the Third Radcliffe was afflicted with gout, presumably of a mild degree, because it rarely interfered with his consultations with royalty or his professional visits to the less fortunate in worldly endowments Radcliffe was a bachelor, highly successful in practice, but mindful of the environment that provided him the opportunity to accumulate wealth By his will he left his possessions to colleges and hospitals The Masters and Fellows of University College, London were bequeathed a trust for the foundation of two traveling fellowships, "The overplus to be paid to them, for the purpose of buying perpetual advowsons for the members of said college" The largest bequest was made to Oxford, for Radcliffe Camera or Library, a smaller sum to St Bartholomew's Hospital to be used "toward mending the diet" In addition to the library, reputed to be the most beautiful building in Oxford, sufficient funds remained to construct the Observatory and the Public Infirmary The latter was opened for reception of patients in 1770

Before the death of Radcliffe, Richard Mead was groomed as the heir apparent to the recipient of the gold-headed cane Mead read Hippocrates and Celsus in the original from his private collection. He questioned the turn of events that would make him the leading physician of physic in London and replied to Radcliffe, "No, Sir when you are gone, your empire, like Alexander's, will be divided among many successors" Mead had been called in consultation by Radcliffe during the last illness of Queen Anne, who found that "her Majesty had been long corpulent, and that, in her latter years, the habit of her body became gross and unwieldy For the most part she had a good stomach, and ate heartily But by reason of her immoderate fatness, and her weakness, occasioned by the gout, she became so inactive that she used but little exercise"

Twenty-five years before Edward Jenner was born, Lady Wortley Montague was determined to introduce the practice of inoculating for the small pox, having had her son inoculated in Constantinople Also, Caroline, Princess of Wales, obtained from his Majesty, George I, permission to inoculate six condemned felons on condition that they be released at the conclusion of the experiment A modification of the Chinese method was practiced upon a seventh criminal, a young girl of eighteen Mead introduced into her nostrils a pledget wetted with matter from a ripe pustule The Chinese practice involved the recovery of skin from dried pustules and the insertion, after moistening, into the nostrils, followed by sealing the nares with wax A notable improvement introduced into clinical medicine by Mead was the application of external pressure to the abdomen during decompression for paracentesis necessitated by abdominal ascites One of Mead's most famous patients was Sir Isaac Newton, who had suffered greatly from stone in the bladder and died, presumably of a "complication" of this malady at the age of 85 years

The next two wearers of the cane were Doctors Askew and Pitcairn Dr Anthony Askew brought bibliomania into fashion He treasured many rare editions and permitted them to be handled only by their owner The Bibliotheca Askeviana was recognized at home and abroad as an outstanding collection Dr Archibald Pitcairn was a brother of Major Pitcairn who was killed in the battle of Bunker Hill The years that he possessed the cane were prolific intellectually and productive medically We know less about Askew and Pitcairn than the last of the five

Matthew Baillie, the last to accept the cane as the mantle of leadership in medical practice, was a nephew of John and William Hunter He emulated his distinguished uncles, he was a teacher of anatomy for more than 20 years 'From his habit of public lecturing, he had acquired two great advantages, First, a minute and accurate knowledge of the structure of the human body, and Second, the most perfect distinctness and excellent arrangement, in what may be called the art of *statement*" Fame came early to Baillie, related partially to his 'Morbid Anatomy," published first in 1793 when he was only 33 years of age After his death, the gold-headed cane, the mace of the English physician, was presented to the College of Physicians where it remains today, a symbol of an era of excellence in the art and practice of medicine

J H T

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1 The Gold Headed Cane ed 2 London J Murray 1828

THE SCHWANN CELL

Theodor Schwann was born near Dusseldorf, Germany in 1810 The description of the cell that covers the nerve fiber made his name familiar to all first-year medical students in their course on neurohistology Researches in recent years into the form and function of the Schwann cell may prompt some physicians to reflect upon the contributions of this 19th century anatomist Schwann was a deeply devout member of the Roman Catholic Church He never married Following his studies at the universities in Wurtzburg and Berlin, he accepted the professorship of anatomy at Louvain, Belgium at the age of 29 Although the eponymic term is his most popular heritage, his greatest contributions were in fermentation and cellular structure For more than 200 years the vegetative cells formed during fermentation were considered to be inanimate bodies Schwann judged them to be living, one of the basic concepts accepted by Pasteur in his earliest investigations in microbiology Schwann also discussed the cell at some length and believed it to be the basic structural unit of animal tissue

The Schwann cell, whose cytoplasm enfolds myelinated and nonmyelinated nerve fibers, has been studied in recent years by a number of investigators who have utilized the electron microscope and modern techniques of tissue culture, with rewarding results The cells have a separate existence and are not syncytial Furthermore, cytoplasmic discontinuity has been demonstrated, with tiny filaments separating the nerve fiber from the cell wall Other studies have concerned the mechanism of myelination, the regeneration of injured nerves, and schwannomas, nerve tumors A monograph on this subject by Causey,[1] currently professor of anatomy in the Royal College of Surgeons in England, details these and other pertinent observations

The epineurium, perineurium, and endoneurium that we studied in neurohistology need not be redefined The revelations of the electron microscope, microbiochemistry, and tissue culture seem more exciting Tissue culture, *in situ*, the regeneration of nerve fibers and their satellite cells (Schwann cell) in the tail of the tadpole, showed that the conjunction of the Schwann cell to the axon of the nerve fiber was a necessary preliminary to myelinization of the axon Also, tissue culture, in vitro, must be maintained for a period of four weeks or longer in order to obtain myelinization The combination of electron microscopy and tissue culture has shown that maturation of the Nissl pattern within the nerve cell body and the deposition of myelin around its peripheral process proceed concomitantly Regeneration of Schwann cells in tissue culture was apparent only after previously, freshly cut normal nerve had been crushed and allowed to degenerate for a few days (Wallerian degeneration)

The motor end-plate has been the object of intensive study with the electron microscope The Schwann cell covers the axon terminally, separating it from the connective tissue in the extracellular space between the end-plate and the nerve fiber The Schwann cell membrane continues over the end-plate and excludes the cytoplasm around the axon from the narrow space that exists between the axon and the muscle cell The axon terminal contains mitochondria and a large number of vesicles that contain acetylcholine The vesicles participate in synaptic transmission and disappear after nerve section at central synapses The diameter of the vesicle, 500 A, seems rather large until it is appreciated that the Angstrom unit is one hundred-millionth of a centimeter The resting potentials of glial cells, that have been examined in tissue culture and also *in situ* in the intact brain of the cat, suggest that the potential recorded in electroencephalography may be produced by the electrical activity of the glial cells in addition to the neuronal electrical charges

The mechanism of nerve regeneration has been an important problem in civilian medicine as well as in military medicine Schwann's original concept of regenerating nerve fiber from coalescence of his cells has been modified somewhat over the years The modern concept is based largely upon electron microscopy, with some contributions from biochemical studies The increase in the nucleic acid content of degenerating peripheral nerve has been attributed to the proliferation of Schwann cells The alteration in total nucleic acid content and the quantity of deoxyribonucleic acid (DNA) appear at an early stage of degeneration, indicating that the nucleic acid proportions begin to alter before cell division The severing of a nerve is followed by changes identified by electron microscopy within 24 to 48 hours The cells in the terminal portion of the proximal stump contribute little or not at all to the bridging of the traumatized area of the nerve Cellular proliferation in the peripheral stump of an injured nerve may be demonstrated after three days and rises to a maximum in three or four weeks Cellular activity is greater distal to the cut than at the proximal end It would seem as if the splintered portion is more concerned with establishing central control than vice versa

Single cells and portions of cells from nerve tumors, schwannomas, have been investigated with the same tools An increase in the proportion of nucleus to cytoplasm, in comparison with normal cells, confirms the findings by light microscopy The cytoplasm in the schwannoma appears to be disintegrating, and there is gross irregularity in the nuclear membrane The membrane may be markedly convoluted, so that in the cell nucleus, not only is there folding of the membrane generally, but the convolutions of the outer nuclear lamina impinge upon the inner lamina This constitutes a distinguishing feature in contrast to the regular parallel lines of the nuclear membrane of the normal cell Several of the studies described by Causey were sponsored by the British Empire Cancer Campaign If any physician is skeptical of the interest shown and the progress made in the study of the form and function of the nerve tissue, reference is made to Causey's monograph on the cell Much progress has been made since the days of the monocular light microscope and the staining of nervous tissue, described by Weigert and Ramón y Cajal

1 Causey, G The Cell of Schwann Edinburgh and London E & S Livingstone Ltd, 1960

LONG-TERM PRESERVATION OF BLOOD

Medical scientists and physicians interested in transfusion problems have worked hard to find ways of storing blood for months or years rather than for the current three or four weeks Effective stockpiling of the large amounts of blood needed for the armed forces and the general population in the event of a nuclear attack would then become possible Blood banks could accumulate rare types of blood and improve their ability to meet special demands, like those of open heart surgery To date, only minor improvements have resulted from changes in the composition of solutions of anticoagulants and preservatives Freezing of red blood cells, which has seemed the most promising attack, has been studied on a limited scale by many workers The technical difficulties, however, are formidable Formation of ice crystals during freezing and thawing must be avoided or cells will be damaged, glycerolization of erythrocytes has been found to prevent formation of crystals, but the glycerol must be removed after thawing before blood can be transfused, asepsis is difficult to maintain, freezing cabinets with adequate controls and auxiliary power units must be devised, techniques successful for freezing small amounts of blood are not necessarily adequate for full transfusion units of about 500 ml Only a few years ago, any practical solution of these problems seemed a remote dream Exciting, therefore, is the report in this issue of THE JOURNAL, p 1657, that the blood bank at the U S Naval Hospital in Chelsea, Mass , under the joint supervision of the Department of the Navy and the Protein Foundation, has succeeded in operating its blood bank with glycerolized frozen blood stored at −80 and −120 C for as long as 44 months

Observations were made with great care The bacteriological control was thorough The loss of cells during processing and storage was not excessive, since an average of 82% of the cells taken from the donor reached the vein of the recipient In vivo survival of the cells was tested in two ways (1) the 24-hour survival after transfusion as a measure of cell viability and (2) the circulating life span of the transfused cells Results were satisfactory on both counts, at least for a storage time of two years The reaction rate was very low The blood was effective in the treatment of shock and anemia and for cardiac surgery, even when placed in a pump oxygenator The suggestion that the incidence of transfusion hepatitis might be reduced by the washing process is interesting, however, as the authors themselves imply, the data are inadequate, and no conclusions are yet justified The cost of operation in terms of manpower and equipment is modest

Many laboratories in the United States and other countries are exploring other ways to freeze and thaw red blood cells, measurement of survival after transfusion is equally meticulous The most important single fact about the Chelsea experience is that the methods have been shown to work in the practical operation of a large transfusion service The Department of Defense is to be commended for its vision in establishing and supporting the glycerolized frozen red blood cell bank under the able supervision of this group of workers The operation needs to be extended and expanded not only at the Chelsea Naval Hospital but at other installations as well Current practices are certainly not the final ones that will evolve The probing for improvement in techniques should be continued until the long term storage of blood becomes a practical reality in many centers

CARL V MOORE, M D
St Louis

Postgraduate Courses for Physicians

Compiled by the Council on Medical Education and Hospitals for the Period Sept 1, 1960, to Aug 31, 1961

The data in the following list of postgraduate courses have been compiled by the staff The Council desires to express appreciation to the officers of the medical schools, hospitals, and medical societies who have cooperated in furnishing the information essential to the preparation of this report

Walter S Wiggins, M D , Secretary
Council on Medical Education and Hospitals

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INTRODUCTION

The sixth annual listing of courses in this country for the continuing education of physicians appears in the following pages of The Journal This listing is for the period September 1 1960 through August 31, 1961

The purpose of the single annual listing is to bring together in one place information secured about continuing medical education (postgraduate) courses to be offered in the year ahead It is the consensus that such a single annual listing provides a reference that potential physician registrants are more likely to consult than do single notices in random issues of The Journal Further, such a list encourages long range advance planning of the courses which, in the opinion of the Council and other medical educators, is likely to contribute significantly to improvement in the quality of the courses so planned During each of the past two years the annual list of postgraduate courses included more than 90% of the courses which ultimately came to the attention of the Council Therefore, it is expected that supplementary notices of postgraduate courses will not be published in The Journal

Continuing medical education (postgraduate) courses consist of planned activities for doctors of medicine intended to refresh practicing physicians in the various aspects of their basic medical education, to provide information on new developments in medicine, and to stimulate further educational efforts by the participants Such courses are not designed to provide the lengthy intensive education required for initial training for a specialty That is graduate medical education, usually comprising residency educational programs Postgraduate courses are shorter than graduate education programs

The following list of courses was prepared from the unappraised and unevaluated replies to Council questionnaires by American medical schools, hospitals and the various national, state and specialty medical societies Unlike the Council's lists of medical schools internships and residencies—which represent approved programs—the following list does not denote either approval or otherwise of the course This is true of necessity because the Council does not at the present time have in operation a mechanism for the appraisal of continuing medical education courses or related programs

This list is printed simply to provide for those physicians seeking to continue their medical education through formal courses a point of departure from which further information can be obtained by writing to the institution or organization listed under Location Inquiries should be made before traveling to any course listed, because dates time arrangements, and fees are subject to change Sponsors of courses having numerical limitation of registrants must restrict enrollment often on the basis of order of application Courses for which there is insufficient registration in advance may be canceled Inquiry of the sponsor is especially urged about courses scheduled for 1961, on which final information may not have been established at the time this list was prepared

Though the educational values of medical society meetings and conventions as well as hospital staff and departmental meetings can be very real and worthwhile, such meetings are not usually listed in the following pages as courses Lists of meetings are to be found periodically elsewhere in The Journal

Many of the courses have co sponsors to whom specific credit cannot be given here because of space limitations It is expected that the institution or organization sponsoring each course has provided such co-sponsor recognition to its registrants

Under each category in the following list, the order of arrangement is alphabetically, first by states second by cities within the state, and third by the institutions and organizations within the cities Last the courses are arranged in the order of the date of the course where several courses in a category are offered by the same institution or organization

Although the list may indicate a course as being designed primarily for specialists in that category some courses so designated are open to any physician This is another reason for specific inquiry to the institution listed

One of the categories has a special use in addition to its usual denotation In the General Medicine category are listed those courses having subjects embracing several fields such as a course on the management of mass casualties or the Summer School of Alcohol Studies

Physicians in general practice should consult all other categories in addition to General Medicine

Following the list of courses appears a geographical cross-reference alphabetically by state and city of the categories under which courses so located are listed This should assist doctors seeking courses in a certain location to find their listing

KEY

Designed For

G—General practitioners
S—Specialists
B—Both
Lim—Enrollment limited to specified number with number stated, i e Lim 20, meaning enrollment limited to 20 in the course If it is repeated, another 20 could be accommodated

Type

IC—Intensive continuous
II—Intensive intermittent
CC—Circuit course
PT—Postgraduate traineeship*
HS—Home study
HS (C)—Home study by correspondence
HS (R)—Home study by radio
O—Other

Time Arrangement

C—Continuous or concentrated (e g , as every day for five days)
I—Intermittent (e g every Thursday for six weeks)

Methods of Education

AV—Audiovisual aids (movies, slides, models)
BR—Bedside rounds
Clin C—Clinical conference
Dem—Demonstrations other than of patients
EPP Enrolee performs procedure
LC—Live clinic
Lab—Laboratory work (including cadaver dissection and dog surgery where applicable)
Lec—Lecture
O—Open question periods
PD—Patient demonstration
Pan—Panel discussion
PT—Postgraduate traineeship*
R—Radio or telephone
Sem—Seminar
Surg—Operative human surgery
TV—Television

* A postgraduate traineeship for practicing physicians is an individually arranged residency type postgraduate educational experience in a hospital usually with residents in that field It differs from a residency or fellowship in the following ways 1 It is not primarily intended to provide training for entering specialty practice or in itself to qualify for specialty board certification 2 Therefore it is of shorter duration than a year 3 It usually does not provide either a stipend or housing and it may exact a fee from the physicians in such training 4 It may not (or may) involve direct patient responsibility

ALLERGY

(See also Basic Sciences, Pediatrics Otolaryngology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Course in Hypersensitivity and Pulmonary Physiology	Children s Hospital of D C 2125 13th St N W Washington 9 D C	S Lim 150	IC	Lec O AV EPP	15	9/30/60	10/ 2/60	C 3 days	50
Hypersensitivity and Allergy	Walter Reed Army Institute of Research Walter Reed Army Medical Center Washington 12 D C	G Lim 10	IC	PD Clin C, Lec O	40	4/17/61	4/21/61	C 5 days	Nil
Asthma, Hay Fever and Allied Diseases	Cook County Graduate School of Medicine 707 S Wood St , Chicago 12	G Lim 5	PT	Lab PD LC BR Lec, O, AV EPP	110	First Monday each mo	Saturday of fourth wk	24 days	500
Personal Course in Allergy	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 3	PT	Lab PD LC BR Lec O AV EPP	600	Arranged	6 mo later	6 mo full time	750
Allergy	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 10	IC	PD, LC, Sem, Lec O, AV	18	4/13/61	4/15/61	C 3 days	40
Allergy for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec, Pan, O AV	15	3/13/61	3/15/61	C, 3 days	40
Allergy	University of Buffalo School of Medicine 3435 Main St , Buffalo	G	IC	PD Sem, Lec, Pan, O, AV EPP	21	3/22/61	3/24/61	C 3 days	45
Medicine PM 68	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	B Lim 10	II	PD LC, Clin C, O	28	9/29/60	1/26/61	I 14 sessions 2 hr weekly Thursdays	50
Pediatric Allergy	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Methodist Hospital Brooklyn, N Y	G Lim 6	II	Lec	12	4/61	5/61	I 6 sessions 2 hr each days unknown	20
Pediatric Allergy	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St , New York	S Lim 15	II	Lab, PD, LC, BR, Clin C, Sem Lec, Pan, O, AV, EPP	240	11/ 2/60	5/31/61	I 30 sessions 8 hr each, days unknown	500
518 Allergy	New York University Post Graduate Medical School 550 First Ave , New York	G Lim 20	IC	Lab PD, Lec O AV	105	10/10/60	10/28/60	C 15 days	250
519 Refresher Course in Allergic Conditions	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	IC	Lab PD Lec, AV	21	3/20/61	3/22/61	C 3 days	65
510 The Management of Allergies	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	II	Lab PD Lec O, AV	16	4/ 7/61	5/26/61	I 8 sessions 2 hr weekly	45
Allergy	Roosevelt Hospital Institute of Allergy 428 W 59th St New York 19	B Lim 25	IC	Lab PD LC BR Clin C Sem Lec Pan O AV EPP	40	5/15/61	5/20/61	C 5½ days	100
Allergy	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G	IC	PD LC Clin C Lec Pan O AV	15	4/17/61	4/18/61	C 2 days	30
Principles of Clinical Allergy	Montefiore Hospital Fifth Avenue Pittsburgh 13	S	IC	Lab PD LC BR Clin C Sem Lec Pan O AV	[illegible]	4/ 3/61	[illegible]	C 1[illegible] days	[illegible]
Clinical Allergy	Montefiore Hospital [illegible]	G	IC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Allergy	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 20	IC	PD LC Clin O Lec Pan O AV EPP	16	11/ 3/60	11/ 4/60	C 2 days	35
Postgraduate Instructional Course in Allergy	The American College of Allergists 2019 Broadway Boulder Colo course at The Statler Hilton Hotel Dallas Texas	B	IC	Lab Clin C Sem Lec Pan O AV	20	3/12/61	3/14/61	C 3 days	50

ANATOMY

(See also Basic Sciences Ophthalmology Surgery)

Gross and Applied Anatomy	San Diego County General Hospital North end of Front Street San Diego 3 Calif	S Lim 20	II	Lab Lec O AV	32	9/60	12/60	I 16 sessions 2 hr weekly Wednesdays	Nil
Surgical Anatomy	St Mary's Hospital 2200 Hayes St San Francisco	S Surg Lim 100	II	Lab PD Clin O Lec	30	9/60 9/61	6/30/61	I 20 sessions 1½ hr biweekly Fridays	Nil
Surgical Anatomy	University of Colorado School of Medicine 4200 E Ninth Ave Denver 20	S Surg Lim 20	IC	Lab Clin C AV	204	Spring 1961	12 wk later	C 12 wk	Unknown
Anatomy 201—Special Dissections in Anatomy	Yale University School of Medicine 333 Cedar St New Haven Conn	S Surg	II	Lab EPP	Arranged	Arranged	Unknown	I Arranged	Arranged
Anatomy 202—Demonstrations in Anatomy	Yale University School of Medicine 333 Cedar St New Haven Conn	S Surg	II	Lab O AV EPP	50	9/60	5/61	I 30 sessions 1½ to 2 hr 1 evening weekly for 30 wk	175
Surgical Anatomy	Harvard Medical School 25 Shattuck St Boston	S Surg Lim 16	IC	Lab Sem Lec AV EPP	140	3/ 6/61	4/28/61	C 40 days	225
General Anatomy Review	Postgraduate Committee University of Maryland School of Medicine 522 W Lombard St Baltimore	S Prep for Surg Exams	Arranged	Lab Lec O	Arranged	Arranged		Arranged	Arranged
Clinical Anatomy	Postgraduate Committee University of Maryland School of Medicine 522 W Lombard St Baltimore	S Surg Lim 20	II	Lab Lec	90	1/25/61	5/61	I 30 sessions 3 hr twice weekly	150
Anatomy	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 50	II	Lab Lec	60	2/16/61	5/25/61	I 4 hr weekly Thursdays	75
Anatomy (Obstetrics and Gynecology)	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	S Lim 40	IC or PT	Lab Lec O	90	4/10/61	4/29/61	C 16 days	75
Anatomy (Surgery)	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	S Lim 40	IC or PT	Lab Lec O PT	Unknown 240	4/10/61 4/10/61	4/29/61 6/ 5/61	C unknown 8 wk	150
Regional Anatomy—Trunk	Wayne State University College of Medicine 1401 Rivard Detroit 7	S Surg Lim 20	II	Lab Lec	64	2/ 7/61	5/31/61	I Unknown	Unknown
Regional Anatomy—Head and Neck	Wayne State University College of Medicine 1401 Rivard Detroit 7	S Surg Lim 20	II	Lab Lec	64	2/ 7/61	5/31/61	I Unknown	Unknown
Regional Anatomy—Back and Limbs	Wayne State University College of Medicine 1401 Rivard Detroit 7	S Surg Lim 40	II	Lab Lec	64	2/ 7/61	5/31/61	I Unknown	Unknown
Surgical Anatomy	Cornell University Medical College 1300 York Ave New York 21	S Surg	IC	Lec O AV EPP	190	5/22/61	6/17/61	C 24 days	200
Gross Human Anatomy for Anesthesiologists Roentgenologists and Surgeons	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 10	IC	Lab O EPP	240	Arranged		C 40 days	300
Gross Human Anatomy for Obstetricians and Gynecologists	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 10	IC	Lab O EPP	84	Arranged		C 14 days	75
Gross Human Anatomy for Orthopedists	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 10	IC	Lab O EPP	84	Arranged		C 14 days	75
Gross Human Anatomy for Otolaryngologists	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 10	IC	Lab O EPP	120	Arranged		C 20 days	125
Gross Human Anatomy for Urologists	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 10	IC	Lab O EPP	84	Arranged		C 14 days	75
Anatomy Surgical (Cadaver Demonstrations)	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 10	II	Lec O EPP	18	10/ 1/60 4/ 1/61	Unknown	I 6 sessions schedule unknown	300

Key will be found on page 1670

ANATOMY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
411 Surgical Anatomy of the Head and Neck	New York University Post Graduate Medical School 550 First Ave New York	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/19/60	12/ 9/60	I, 36 sessions 4 hr thrice weekly Mondays Wednesdays Fridays	100
412 Surgical Anatomy of the Thorax and Its Viscera	New York University Post Graduate Medical School 550 First Ave, New York	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/19/60	12/ 9/60	I 36 sessions 4 hr thrice weekly Mondays Wednesdays Fridays	100
413 Surgical Anatomy of the Abdomen	New York University Post Graduate Medical School 550 First Ave New York	G Lim 12	II	Lab, Sem, Lec, AV EPP	144	9/19/60	12/ 9/60	I 36 sessions 4 hr thrice weekly Mondays Wednesdays Fridays	100
583 Anatomy for Orthopedic Surgeons	New York University Post Graduate Medical School 550 First Ave New York	S Lim 20	IC	Lab O, EPP	35	1/ 9/61	1/13/61	C 5 days	165
414 Surgical Anatomy of the Female Pelvis	New York University Post Graduate Medical School 550 First Ave New York	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	3/20/61	6/ 9/61	I, 36 sessions 4 hr thrice weekly Mondays Wednesdays Fridays	100
415 Surgical Anatomy of the Genitourinary System	New York University Post Graduate Medical School 550 First Ave New York	G Lim 12	II	Lab, Sem Lec, AV, EPP	144	3/20/61	6/ 9/61	I 36 sessions 4 hr thrice weekly days not determined	100
416 Surgical Anatomy of the Musculoskeletal System	New York University Post Graduate Medical School 550 First Ave, New York	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	3/20/61	6/ 9/61	I 36 sessions 4 hr thrice weekly, days not determined	100
Regional Anatomy	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center, Houston 25 Texas course at M D Anderson Hospital and Tumor Institute, Houston 25 Texas	G Lim 12	II	Surg, Lec EPP	80	9/ 1/60	6/29/61	I 40 sessions 2 hr weekly, Thursdays	100

ANESTHESIOLOGY

(See also Anatomy, Cardiovascular Disease, Chest Diseases)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Spring Postgraduate Meeting	Anesthesia Section Los Angeles County Medical Society 686 E Union St Pasadena Calif	S	IC	Sem, Lec, Pan, O	10	Unknown	Unknown	C Unknown	20
Second Biennial Connecticut Postgraduate Anesthesia Seminar	Connecticut State Society of Anesthesiologists 125 Walbridge Rd West Hartford 7 Conn course at Hartford Medical Society Hartford Conn	S	IC	Sem, Lec, Pan, O AV	12	5/ 5/61	5/ 6/61	C, 2 days	25
Course I—Regional Anesthesia	Cook County Graduate School of Medicine 707 S Wood St, Chicago 12	G Lim 1	PT	PD LC BR, Surg Lec O AV, EPP	140	First Monday each mo	Friday of fourth wk	20 days	300
Course V—Inhalation and Endotracheal Anesthesia	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 1	PT	PD LC BR, Surg Lec O, AV EPP	140	First Monday each mo	Friday of fourth wk	20 days	300
Medical Traineeship in Anesthesiology	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	PT	PD Lec EPP	160	Each Monday	Variable	28 days	150
Anesthesiology for the Full and Part Time Anesthetist	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G Lim Varies	IC	Lec, O, AV	14	3/ 1/61	3/ 2/61	C, 2 days	25
Anesthesiology	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	Lec Pan, O, AV	10	3/17/61	3/18/61	C 1½ days	20
Clinical Traineeship in Anesthesiology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City, Kan	B Lim 1	P1	BR Clin C Sem, Lec, O AV, EPP	Unknown	Arranged	Unknown	Unknown	0 mo Kansas residents 100 mo nonresidents
Anesthesiology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	Lec Pan, O, AV	21	4/17/61	4/19/61	C, 3 days	45
Anesthesiology	Maine Medical Center 22 Bramhall St Portland Maine	G Lim 3	P1	PD Clin C Sem Lec O AV EPP	Arranged	Arranged		Individually arranged	Nil
Principles of Anesthesiology	Wayne State University College of Medicine 1401 Rivard Detroit	S	II or PT	Lab Clin C Lec	72	9/14/60 Annually	6/14/61	I schedule unknown	40
Anesthesiology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	S	IC	PD Lec Pan O AV	15	2/ 6/61	2/ 8/61	C 3 days	40

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Anesthesiology	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IC	PD Sem Lec Pan O AV	6	5/ 2/61	5/ 2/61	C 1 day	15
Anesthesia	University of Buffalo School of Medicine 3435 Main St Buffalo	G Lim 12	IC	PD Sem Lec Pan O AV EPP	39	4/10/61	4/15/61	C 5½ days	75
Endotracheal Techniques in Anesthesia	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Division New York 29	G Lim 10	IC	PD Sem Lec AV EPP	45	Arranged	One wk later	C 5 days	125
Special Techniques in Anesthesia	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Center New York 29	C Lim 10	IC	PD Sem Lec AV EPP	45	Arranged	One wk later	C 5 days	125
Diagnostic and Therapeutic Nerve Blocks	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Center New York 29	G Lim 10	IC	PD Sem Lec AV EPP	45	Arranged	One wk later	C 5 days	125
Anesthesia and Analgesia in Obstetrics	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Division New York 29	C Lim 10	IC	PD Sem Lec AV EPP	45	Arranged Every Monday	One wk later	C 5 days	125
Applied Anesthesiology	New York Polyclinic Hospital 345 W 50th St New York	G Lim 10	IC	PD BR Lec EPP	480	10/ 1/60 4/ 1/61	12/31/60	C 72 days	300
512 Anesthesiology (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 2	IC	PD Clin C Surg Lec EPP	70	Any Monday September through June		C 10 days	175
13 Regional Anesthesiology	New York University Post Graduate Medical School 550 First Ave New York	G Lim 16	IC	Lab Lec EPP	42	9/12/60 1/ 9/61 4/17/61	9/17/60	C 6 days	135
11 Anesthesiology Endotracheal and Related Methods	New York University Post Graduate Medical School 550 First Ave New York	S Lim 4	IC	Lab PD Clin C Surg Lec EPP	35	9/26/60 1/23/61 3/20/61	10/ 1/60	C 5 days	135
Postgraduate Traineeship	Duke Medical Center Box 3535 Duke Hospital Durham N C	G Lim 2	PT	PD LC BR Clin C Sem Lec EPP	Arranged	Arranged		Arranged	Nil
Postgraduate Refresher Course	Duke Medical Center Durham N C	G Lim 50	IC	PD LC BR Clin C Lec Pan O EPP	25	5/61		C 3 days	25
Recent Advances in the Physiologic Aspects of Anesthesia	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	G	IC	Sem Lec Pan O AV		2/ 6/61	2/ 8/61	C 3 days	75
Basic Science in Anesthesiology	Department of Anesthesiology University of Pittsburgh School of Medicine School of Health Professions Building DeSota and Terrace Streets Pittsburgh 13	B Lim 50	IC	Lab Clin C Lec Pan O	51	6/12/61	6/16/61	C 5 days	50
Anesthesiology for the General Practitioner	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap Memphis Tenn	G Lim 4	PT	PD LC Clin C Sem Lec Pan O AV EPP	40	9/26/60	9/30/60	5 days	65
Anesthesiology for the General Practitioner	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap Memphis Tenn	G Lim 20	IC	PD LC BR Clin C Sem Lec Pan O AV EPP	23	3/22/61	3/24/61	C 3 days	55
Sixth Annual Course in Anesthesiology	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	B Lim 270	IC	Lec Pan O AV TV EPP	20	3/ 8/61 Annually	3/10/61	C 3 days	45
Postgraduate Refresher Course in Anesthesiology	Scott and White Memorial Hospital and Scott Sherwood and Brindley Foundation Temple Division University of Texas Postgraduate School of Medicine 213 W Avenue G Temple Texas	C Lim 1	PT	PD BR Sem Surg Lec EPP	176	First Monday of mo September through May	Last Saturday of mo	24 days	25
Anesthesiology	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at Scott and White Clinic Temple Texas	G Lim 2	PT	PD BR Sem Surg Lec O EPP	172	9/ 5/60 First Monday each mo through 5/61	9/30/60	23 days	25

Key will be found on page 1670

BASIC SCIENCES

(See also Anatomy, Clinical Pathology, Pathology, Radioisotopes)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Statistical Methods in Psychological Research	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant St, Palo Alto, Calif	S Lim 20	II	Sem Lec, O	10	10/ 8/60	12/ 3/60	I 5 sessions 2 hr weekly Saturday	Unknown
Correlation of Medical Basic Sciences	St Mary's Hospital 2200 Hayes St, San Francisco	G Lim 400	II	Clin C, Lec, O	20	9/60 9/61	6/30/61	I 20 sessions 1 hr biweekly, Saturdays	Nil
Microbiology 210—Diagnostic Medical Mycology	Yale University School of Medicine 333 Cedar St New Haven Conn	S	IC	Lab, Sem, O, EPP	70	Arranged	Unknown	C 10 days (5 days a wk for 2 wk)	100
Introduction to Research Methods	Armed Forces Institute of Pathology 6825 16th St N W, Washington 12, D C	B Lim 120	IC	Lec, O, AV, TV, EPP	35	3/27/61	3/31/61	C 5 days	Nil
15th Annual Postgraduate Course on Clinical Cardiopulmonary Physiology	American College of Chest Physicians 112 E Chestnut St, Chicago course at Sheraton Towers Hotel Chicago	B Lim 100	IC	Lec, Pan, O, AV	35	10/24/60 10/61	10/28/60	C 5 days	75 for members 100 for non-members
Clinical Traineeship in Microbiology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 1	PT	Lab, PD LC BR Clin C Sem, Lec, O AV FPP	Unknown	Arranged	Unknown	Unknown	50 mo Kansas residents 100 mo non residents
Conference on Medical Education	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City, Kansas	S	IC	Sem, Lec, Pan, O, AV	21	8/29/60	8/31/60	C 3 days	Nil
Histochemistry	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City Kansas	S Lim 18 1st wk 30 2nd wk	IC	Lab Sem, Lec, O, AV, FPP	84	6/ 5/61	6/17/61	C 12 days	150 or 75 for 1 wk
Basic Sciences as They Apply to the Practice of Medicine	Postgraduate Committee University of Maryland School of Medicine 522 W Lombard St, Baltimore	G Lim 100	II	Lec	42	1/ 4/61	5/24/61	I Unknown	50
Basic Science Correlations in Disease States	Postgraduate Medical Institute 22 Fenway Boston 15 course at Jimmy Fund Building Auditorium Boston	B	II	Lec, AV	31½	9/22/60	3/ 2/61	I 21 sessions 1½ hr weekly, Thursdays	50 practicing physicians 15 interns and residents
Basic Sciences with Clinical Application	The University of Michigan Medical Center *Department of Postgraduate Medicine* University Hospital Ann Arbor Mich	S res Lim 40	IC	Lab PD, LC, Clin C, Lec, O, AV	Full Time	9/26/60	6/ 2/61	C 170 (8 mo)	500
Bacteriology with Clinical Aplication	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	S Lim 40	IC	Lab PD Clin C, Lec O AV	60	1/ 2/61	1/13/61	C 10 days	50
Biophysics with Clinical Application	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	S Lim 40	IC	Lab Clin C, Lec, O, AV	60	1/16/61	1/27/61	C 10 days	50
Biochemistry with Clinical Application	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	S Lim 40	IC	Lab, PD Clin C Lec, O AV	90	2/13/61	3/ 3/61	C 15 days	75
Physiology with Clinical Correlation	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	S Lim 40	IC	Lab, PD, Clin C, Lec O AV	60	3/ 6/61	3/17/61	C 10 days	50
Pharmacology with Clinical Application	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	S Lim 40	IC	Lab, PD Clin C, Lec Pan, O AV	60	3/20/61	3/31/61	C 10 days	50
Physiology of Respiration	Wayne State University College of Medicine 1401 Rivard Detroit 7	B Lim 12	II	Lab Sem Lec, O AV FPP	96	9/60	2/61	I 32 sessions schedule unknown	90
Physiology Seminar	Wayne State University, College of Medicine 1401 Rivard Detroit 7	B	II	Sem	32	9/60 Annually	2/61 or 6/61	I 32 sessions schedule unknown	45
Cellular Physiology	Wayne State University College of Medicine 1401 Rivard Detroit 7	B Lim 16	II	Lab Lec, O, AV	96	9/60	2/61	I 32 sessions schedule unknown	90
Seminar in Physiological Chemistry	Wayne State University College of Medicine 1401 Rivard, Detroit 7	B Lim 40	II	Sem	16	9/60	2/61	I schedule unknown	22 50
Physiology of Reproduction	Wayne State University College of Medicine 1401 Rivard Detroit 7	B	II	Sem Lec O AV	32	9/60	2/61	I schedule unknown	45
Cytochemistry	Wayne State University College of Medicine 1401 Rivard Detroit 7	B Lim 12	II	Lab Lec	80	2/61	6/61	I schedule unknown	45
Nutritional Biochemistry	Wayne State University College of Medicine 1401 Rivard Detroit 7	B Lim 150	II	Lec	32	2/61	6/61	I schedule unknown	67 50
Survey of Advances in Physiology	Wayne State University College of Medicine 1401 Rivard Detroit 7	B	II	Sem Lec AV	16	2/61 Yearly—even numbered years	6/61	I 16 sessions 1 hr weekly days unknown	22 50

Application of Biochemistry and Physiology to Clinical Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark N J	C Lim 4	II	Lec O AV	22	9/21/60	1/11/61	I 1 sessions 1¼ hr weekly Wednesdays	[illegible]
Clinical Dialysis	University of Buffalo School of Medicine 3435 Main St Buffalo	G Lim 30	IC	Lab PD Sem Lec Pan O AV EPP	14	11/ 2/60	11/ 3/60	C 2 days	30
Mechanisms of Disease	American College of Physicians 4200 Pine St Philadelphia 4 course at Columbia University College of Physicians and Surgeons New York	S	IC	PD Clin C Sem Lec Pan	40	1/16/61	1/20/61	C 5 days	60 members 80 non members
Physiology PM 33—Seminar in Selected Topics in Gastrointestinal Physiology	Columbia University College of Physicians and Surgeons 630 W 168 St New York 32 course at Mount Sinai Hospital New York 29	C	II	Sem O AV	60	10/60	[illegible]/61	I 1 hr twice weekly	Unknown
Physiology PM [illegible]	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	II	Lec O AV	52	10/ 5/60	4/ 5/61	I 26 sessions 2 hr weekly Wednesdays	150
Correlated Clinical Science Course	The New York Academy of Medicine 2 E 103rd St New York 29	G	II	Sem O AV	70	9/ 6/60	5/23/61	I 35 sessions 2 hr each days unknown	Nil
Biochemistry—Protein Metabolism	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	B Lim 20	II	Lec O	16	Unknown		I 8 sessions 2 hr each	75
Biochemistry—Lipid Metabolism	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	B Lim 20	II	Lec O	16	Unknown		I 8 sessions 2 hr each	75
Biochemistry—Radioactivity and Metabolism	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	B Lim 20	II	Lec O	16	Unknown		I 8 sessions 2 hr each	[illegible]
Biochemistry—Biochemistry of the Digestive System	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	B Lim 20	II	Lec O	16	Unknown		I 8 sessions 2 hr each	75
Biochemistry—Chemistry and Biochemistry of Connective Tissues	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G Lim 20	II	Lec O	16	Arranged		I 8 sessions 2 hr each days unknown	75
Review of Embryology—Practical Considerations in Developmental Anomalies	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G Lim 15	II or IC	Lec AV	15	2/ 2/61	4/ 6/61	I 10 sessions 1½ hr each O arranged	100
Basic Sciences in Medicine and Surgery	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 20	IC	Lab PD LC BR Clin O Sem Lec O AV EPP	30	10/ 1/60 4/ 1/60	10/ 7/60	C 6 days	50
[illegible] Toxicology	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians Lim 6	IC	Lab Sem Lec AV EPP	Vary according to registration period	Arranged	Varies	C varies	100 per mo
[illegible] Neuroanatomy and Neurophysiology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 50	II	Lab Lec	126	9/12/60		I 36 sessions 3½ hr thrice weekly Mondays Wednesdays Fridays	375
[illegible] Comprehensive Review in Dermatologic Histopathology	New York University Post Graduate Medical School 550 First Ave New York	C Lim 15	IC	Lab Sem Surg Lec Pan O AV EPP	35	9/26/60	9/30/60	C 5 days	100
[illegible] Clinical Physiology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 35	II	Lec O AV	16	3/ 1/61	4/19/61	I 8 sessions 2 hr weekly Wednesdays	75
Muscle as a Tissue	Lankenau Hospital Lancaster Avenue and City Line Philadelphia 31	S	IC	Lab PD Clin C Sem Lec Pan O AV TV EPP	12	11/ 3/60	11/ 4/60	C 2 days	Nil
Correlated Basic Sciences	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	C Lim 25	IC	Lab Sem Lec Pan O	192	9/20/60	1/20/61	C Unknown	250
Practical Biostatistics for the Practicing Physician	Department of Preventive Medicine Woman's Medical College of Pennsylvania Henry Avenue and Abbottsford Road Philadelphia	B Lim 10	II	Lec O	8	10/60	11/60	I 4 sessions 2 hr weekly Wednesday evenings	15

Key will be found on page 1670

BASIC SCIENCES—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Basic Science Seminars	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg, Texas Medical Center Houston Texas course at St Luke's Episcopal Hospital, Houston, Texas	G and Residents	II	AV	15	2/10/61 Annually	5/19/61	I 15 sessions 1 hr weekly, Fridays	Unknown
Immunology in Clinical Medicine	University of Washington School of Medicine Seattle	B	IC	Sem Lec Pan, O, AV	Unknown	11/10/60	11/12/60	C 2½ days	Unknown
Principles and Techniques of Tissue Culture	Dr Mary S Parshley, Registrar Tissue Culture Association 630 W 168th St, New York 32 course at University of Wisconsin Department of Zoology, Madison, Wis	S Lim 30	IC	Lab, Sem, Lec FPP	114	6/19/61	7/14/61	C, 26 days	100

CARDIOVASCULAR DISEASE

(See also Chest Diseases, Electrocardiography, General Medicine, Internal Medicine)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Thirtieth Annual Professional Symposium	Los Angeles County Heart Association 2405 W Eighth St Los Angeles 57 course at Beverly Hilton Hotel Beverly Hills Calif	G	IC	Sem Lec, Pan, O, AV	16	10/ 5/60 10/61	10/ 6/60	C 2 days	Unknown
Symposium on Heart Disease	Orange County Heart Association P O Box 1704 Santa Ana Calif	G	IC	Lec Pan O AV	8 to 10	Spring	Same Day	C 1 day	15
Fifth Annual Symposium on Cardiovascular Disease	Santa Barbara County Heart Association 18 La Arcada Court Santa Barbara Calif course at Biltmore Hotel Santa Barbara Calif	G	IC	Clin C Sem Lec, Pan O, AV	6	9/17/60	9/17/60	C 1 day	25
30th Annual Symposium on Cardiovascular Disease	San Francisco Heart Association 259 Geary St San Francisco course at St Francis Hotel San Francisco	B	IC	Sem Lec Pan O AV	21	10/5 /60 9/27/61	10/ 7/60	C 3 days	25 for all 3 days 5 per half day session
Postgraduate Course for Physicians	Contra Costa County Heart Association 2030 N Main St, Walnut Creek, Calif course at Contra Costa County Hospitals Martinez Calif	G Lim 100	II	Lec, Pan AV	16	2/ 6/61	3/27/61	I Unknown	10
Western Cardiac Conference	Colorado Heart Association 1636 Logan St, Denver 3	G	IC	Clin C, Lec Pan O AV	30	Unknown		C, 5 days	30
International Seminar on Myocardial Metabolism	Heart Association of Greater Miami, Inc 253 S W Eighth St, Miami 32 Fla course at Americana Hotel Miami Beach Fla	S Lim 400	IC	Sem Lec, Pan	35	10/19/60	10/21/60	C 3 days	Unknown
The Physical Examination of the Heart (Inspection Palpation and Auscultation)	Department of Internal Medicine Emory University School of Medicine 69 Butler St, S E Atlanta 3 Ga course at Grady Memorial Hospital Auditorium, Atlanta 3 Ga	G	IC	PD, Clin C, Sem Lec Pan, O AV, EPP	16	3/10/61	3/11/61	C 2 days	Unknown
Twelfth Annual Scientific Sessions Georgia Heart Association	Georgia Heart Association Inc 1101 W Peachtree St N E Atlanta 9, Ga course at General Oglethorpe Hotel Savannah Ga	G	IC	Lec, Pan O, AV	8	9/ 9/60	9/10/60	C 2 days	Nil
Treatment of Arteriosclerotic Disease	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec Pan, O AV	7	1/25/61	1/25/61	C 1 day	10
10th Annual Heart Symposium	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec Pan, O AV	7	2/15/61	2/15/61	C, 1 day	Nil
Cardiology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 10	PT	Lab PD, LC BR Clin C Sem, Lec, O AV FPP	Unknown	9/15/60	6/15/61	9 mo	600
Clinical Traineeship in Cardiovascular Disease	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 2	PT	Lab LC BR Clin C Sem Lec O AV EPP	120	2/ 1/61 3/ 1/61	2/28/61	30 days	50 mo residents of Kansas 100 mo non residents
Cardiac Auscultation	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 20	IC	LC Clin C Lec O AV	14	5/ 8/61	5/ 9/61	C 2 days	50
Seventh Annual Symposium on Cardiovascular Diseases	The Heart Association of Louisville and Jefferson County and University of Louisville Medical School 311 Speed Bldg Louisville Ky course at Brown Hotel Louisville Ky	G	IC	Sem	10	3/22/61	3/23/61	C 2 days	Unknown

Postgraduate Course in Heart Disease	Heart Association of Maryland 1140 Mondawmin Baltimore 15 course at University of Maryland School of Medicine Baltimore 3	G	IC	PD BR Clin C Lec Pan AV EPP	16	1/61	1/61	C 3 days	30 including meals
Course in Cardiovascular Diseases	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston 14	G Lim 14	IC	PD LC BR Clin C Sem Surg Lec O AV EPP	804	10/ 1/60 10/ 1/61	5/31/61	C 7 mo	800
Cardiovascular Disease	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	S Lim 14	IC	PD LC Clin C Sem Lec O EPP	904	10/ 3/60	5/31/61	C Unknown	800
Cardiology 1	Harvard Medical School 25 Shattuck St Boston course at Beth Israel Hospital Boston	S Lim 12	IC	Lab PD LC BR Clin C Sem Lec O AV EPP	500	2/ 1/61	4/29/61	C 76 days	500
Cardiology	The University of Michigan Medical Center Department of Postgraduate Medicine 1010 University Hospital Ann Arbor Mich	G Lim 60	IC	Lab PD Lec Pan O AV	40	3/13/61	3/17/61	C 5 days	50
Diseases of the Heart	The University of Michigan Medical Center Department of Postgraduate Medicine 1010 University of Michigan Ann Arbor Mich	G Lim 40	IC	PD Clin C Lec O AV	34	3/20/61	3/24/61	C 5 days	50
Cardiovascular Seminar	The University of Mississippi School of Medicine University Medical Center Jackson Miss	B Lim 150	IC	PD BR Clin C Sem Lec Pan O AV TV	20	4/ 5/61	4/ 7/61	C 3 days	10
A Morris Ginsberg Memorial Seminar	Menorah Medical Center 4949 Rockhill Rd Kansas City Mo	B	IC	PD BR Clin C Lec Pan O AV	14	12/ 1/60	12/ 2/60	C 2 days	Nil
Session on Clinical Cardiology	American Heart Association 44 E 23rd St New York course at Kiel Auditorium St Louis	G	IC	Lec Pan O AV	18	10/21/60	10/23/60	C 3 days	3
Acute Cardio Respiratory Failure with Resuscitation	Seton Hall College of Medicine and Dentistry Medical Center 24 Baldwin Ave Jersey City 4 N J course at St Michael's Hospital Newark N J	B Lim 12	IC	Lec O AV EPP	6	10/60 Monthly	10/60	C 1 day	35
Recent Advances in Clinical Cardiology	Seton Hall College of Medicine and Dentistry Medical Center 24 Baldwin Ave Jersey City 4 N J course at St Michael's Hospital Newark N J	G Lim 60	II	PD LC BR Clin C Lec O AV	24	10/60	3/61	I 12 sessions 2 hr alternate Wednesdays	40
Resuscitation of the Arrested Heart Including Surgical Technique	Booth Memorial Hospital 56 45 Main St Flushing 55 N Y	S	IC	Lab Sem Lec O	6	10/ 1/60	10/ 1/60	C 1 day	Unknown
Medicine PM 60—Cardiology I Elementary	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G	II	PD Surg Lec O AV EPP	96	9/29/60 2/ 9/61	2/ 2/61	I 16 sessions 6 hr weekly Thursdays	150
Medicine PM 62—Cardiology II Advanced	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G	II	PD LC Lec Pan O AV EPP	56	9/29/60 2/ 9/61	2/ 2/61	I 16 sessions 3½ hr weekly Thursdays	150
Medicine PM 29—Clinical Cardiology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mt Sinai Hospital New York 29	G	II	PD LC BR Lec O	20	10/18/60 2/ 7/61	12/20/60	I 10 sessions 2 hr weekly Tuesdays	60
Medicine PM 31—Recent Advances in Cardiovascular Disease	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mt Sinai Hospital New York 29	G	IC	Lab PD Clin C Lec O AV EPP	30	1/23/61	2/ 3/61	C 10 days	75
Medicine PM 48—Heart Disease and Circulatory Dynamics	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mt Sinai Hospital New York 29	G Lim 10	II	PD LC BR Lec O AV EPP	20	2/14/61	4/18/61	I 10 sessions 2 hr weekly Tuesdays	50
E C G Interpretation	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Beth El Hospital Brooklyn N Y	G Lim 12	II	LC Lec	12	10/60	11/60	I 12 sessions 1 hr each days unknown	20
Clinical Cardiology	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Coney Island Hospital Brooklyn N Y	G Lim 30	II	PD Lec	15	10/60	12/60	I 10 sessions 1½ hr each days unknown	30
Recent Advances in Diagnostic Procedures	New York State Heart Assembly 105 E 22nd St New York 10 course at Hotel Statler Hilton Buffalo	G Lim 600	IC	Lec Pan O AV	5	Unknown	Unknown	C 1 day	Nil

Key will be found on page 1670

CARDIOVASCULAR DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
47 Diagnostic Cardiac Auscultation	New York University Post Graduate Medical School 550 First Ave, New York	G Lim 40	IC	Lab PD, Lec O AV	24	10/12/60 3/ 1/61	10/15/60	C 4 days	60
Seminars on Heart Disease	St Francis Hospital and Sanatorium Roslyn, N Y	G Lim 75	II	Sem Lec O	8	9/60	5/61	I 4 sessions 2 hrs bimonthly, Thursdays	Nil
Postgraduate Course in Cardiology—Congenital Heart Disease	St Francis Hospital and Sanatorium Roslyn, N Y	G Lim 60	IC	PD Sem Lec Pan O, AV TV, EPP	18	10/13/60 Spring 1961	10/15/60	C 3 days	Unknown
Heart Disease—With Emphasis on Newer Diagnostic Techniques—Medical and Surgical Management	University of Cincinnati College of Medicine—Cardiac Laboratory Eden and Bethesda Avenues Cincinnati 19 course at Cincinnati General Hospital, Cincinnati 29	G Lim 75	IC	PD, LC Clin C Sem Lec AV EPP	23	9/ 7/60 Annually	9/10/60	C, 3½ days	75
Cardiac Arrest and Resuscitation	Mercy Hospital Research Foundation 2221 Madison Ave, Toledo, Ohio	B Lim 15	IC	Lab Lec, O AV EPP	4	9/28/60	9/28/60	C 1 day	Nil
Cardiovascular Diseases	American College of Physicians 4200 Pine St Philadelphia 4 course at Mt Sinai Hospital	S	IC	PD Clin C Sem Lec Pan	40	3/ 6/61	3/10/61	C 5 days	60 members, 80 non members
Postgraduate Cardiology—Electrocardiography Cardiac Therapy Cardiac Auscultation	Hahnemann Medical College and Hospital 230 N Broad St Philadelphia	G Lim 30	II	PD Lec, O AV	60	10/ 1/60	5/26/61	I 30 sessions 2 hr weekly	225
Coronary Artery Disease	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas	G Lim 200	IC	Lec AV	20	11/28/60	12/ 2/60	C 5 days	Unknown
Annual Symposium of Washington State Heart Association—Diagnosis and Management of Heart Disease and Strokes	Washington Heart Association and State Department of Health 3121 Arcade Bldg Seattle 1 course at University of Washington Seattle 5	G Lim 500	IC	Sem Lec O	9	10/14/60	10/15/60	C 2 days	Unknown

CHEST DISEASES

(See also Cardiovascular Disease)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Sixth Annual Postgraduate Course on Diseases of the Chest	American College of Chest Physicians 112 E Chestnut St Chicago course at Jack Tar Hotel San Francisco	B Lim 100	IC	Lec Pan O AV	35	12/ 5/60 12/61	12/ 9/60	C 5 days	75 for members 100 for non members
Symposium on Pulmonary Disease	Fitzsimons General Hospital Denver Colorado	G Lim 100	IC	PD, LC Clin C Lec Pan O, AV EPP	40	9/19/60	9/23/60	C 5 days	Unknown
13th Annual Symposium on Pulmonary Diseases	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20 course at Fitzsimons General Hospital Denver	B	IC	Sem Lec Pan O AV	40	9/19/60	9/23/60	C 5 days	5
Diagnosis and Management of Cardiopulmonary Diseases	Yale University School of Medicine 333 Cedar St New Haven, Conn	G Lim 100	II	Clin C Lec AV	18	10/27/60	12/15/60	I 7 sessions 2½ hr weekly Thursdays	35
Non Tuberculous Pulmonary Disease	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec, O AV	7	1/11/61	1/11/61	C 1 day	10
Clinical Traineeship in Pulmonary Disease	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City, Kan	B Lim 2	PT	Lab, LC BR Clin C Sem Lec O AV EPP	160	11/ 1/60 1/ 2/61 4/ 1/61 5/ 2/61	11/30/60	30 days	50 mo Kansas residents 100 mo non residents
Pulmonary Disease (Medical Surgical Clinical Symposia)	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD LC Lec Pan O AV	7	3/20/61	3/20/61	C 1 day	20
Journal Club and Tissue Committee Meetings	State Tuberculosis Hospital Hazelwood Sanatorium Louisville Ky	S	II	Sem	36	9/20/60 Annually	8/15/61	I 12 sessions 3 hr 3rd Tuesday each mo	Nil
Louisville Chest Group Meetings	State Tuberculosis Hospital Hazelwood Sanatorium Louisville Ky	S	II	Sem	18	9/28/60 Annually	5/24/61	I 6 sessions 3 hr 4th Wednesday each mo	Nil
The Measurement of Pulmonary Function in Health and Disease	Dr Edward J Welch Chairman American Trudeau Society 1101 Beacon St Brookline 46 Mass course at Boston City Hospital Boston Mass	S Lim 150	IC	PD LC Clin C Sem Lec Pan O AV EPP	40	3/20/61	3/24/61	C 5 days	100
Pulmonary Diseases	The University of Michigan Medical School Department of [illegible] Medicine The University Hospital Ann Arbor Mich	G Lim [illegible]	IC	Lab PD Clin C Lec O AV	18	4/10/61	4/[illegible]/61	C [illegible] days	40

13th Annual Postgraduate Course—Recent Advances in Treatment of Diseases of the Lung and Heart	American College of Chest Physicians 112 E Chestnut St Chicago course at Park Sheraton Hotel New York	B Lim 100	IC	PD PC Lec Pan O AV	3[illegible]	11/14/60 11/61	11/18/60	C 5 days	75 for members 100 for non members
Medicine PM 80	Columbia University 630 W 168th St New York 32 course at Bellevue Hospital New York 32	S Lim [illegible]	IC	BR Clin C Lec O AV	161	10/ 3/60 2/ 1/61	10/31/60	C 23 days	175 first mo 75 for additional periods
Medicine PM 81	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	C Lim 30	II	PD BR Clin C Sem Lec O AV	52½	1/10/61	5/23/61	I 21 sessions 2½ hr weekly Tuesdays	100
612 Symposium on Tuberculosis and Other Pulmonary Diseases in Children	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 18	IC	PD PC Lec Pan O AV	35	4/ 3/61	4/ 7/61	C 5 days	75
Symposium for General Practitioners on Tuberculosis and Other Pulmonary Diseases	Saranac Lake Medical Society P O Box 627 Saranac Lake N Y course at Saranac Laboratory Saranac Lake N Y	G Lim 75	IC	PC BR Clin C Lec Pan O AV	27	7/11	5 days later	C 5 days	60
Chronic Pulmonary Disease	Glenridge Hospital 175 Glenridge Rd Schenectady N Y	G Lim 30	II	PD Sem O AV	12	9/60	4/61	I 8 sessions 1 day each mo	Nil
Cardiopulmonary Diseases	Department of Research—St Joseph's Hospital 301 Prospect Ave Syracuse N Y	G	IC	Clin C Lec Pan O AV	6	11/60		C 1 day	Unknown
Post Graduate Course in Pulmonary Diseases	Ohio TB and Health Association 1575 Neil Ave Columbus course at College of Medicine Ohio State University Columbus 10	C Lim 150	IC	Sem Lec	11	9/22/60	9/23/60	C 2 days	25
11th Annual Postgraduate Course on Diseases of the Chest	American College of Chest Physicians 112 E Chestnut St Chicago course at Sheraton Hotel Philadelphia	B Lim 100	IC	Lec Pan O AV	35	3/27/61 3/62	3/31/61	C 5 days	75 for members 100 for non members
Bronchoesophagology	Temple University School of Medicine and Hospital 3400 N Broad St Philadelphia 40	B Lim 20	IC	Lab PD PC Clin C Sem Lec Pan O FPP	80	11/ 7/60 2/ 6/61	11/18/60	C 11 days	250
Chest and Infectious Diseases	University of Washington School of Medicine Seattle	B	IC	Lec Pan O AV	Unknown	12/60	Unknown	C 2 days	Unknown
Pathology and Radiology of Chest Diseases	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at Wisconsin Center Building Madison 6 Wis	S	IC	PD PC Clin C Sem Lec Pan O AV FPP	17½	5/11/61	5/12/61	C 2½ days	50

CLINICAL PATHOLOGY

Clinical Laboratory Interpretation	University Extension—University of California Los Angeles University of California Medical Center Los Angeles	B	IC or II	Sem Lec Pan O AV	18	1/61	Unknown	C unknown I unknown	40
Laboratory Methods in the Diagnosis of Malaria (805)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 2	IC	Lab EPP	40	Arranged		C 5 days	Nil
Special Training in Virus Techniques (8[illegible]1)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 8	IC	Lab EPP	80 to 160	Arranged		C 10 to 20 days	Nil
Typing of Corynebacterium Diphtheriae (812)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 2	IC	Lab EPP	40	Arranged		C 5 days	Nil
Special Problems in Enteric Bacteriology (851)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 3	IC	Lab FPP	80	Arranged		C 10 days	Nil
Phage Typing of Salmonella Typhosa (8[illegible])	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 2	IC	Lab EPP	40	Arranged		C 5 days	Nil
Laboratory Methods in the Diagnosis of Leptospirosis (858)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 2	IC	Lab EPP	40 to 160	Arranged		C 5 to 20 days	Nil
Serologic Differentiation of Streptococci (851)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 2	IC	Lab EPP	80	Arranged		C 10 days	Nil
Special Problems in Microbiology (81[illegible])	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 2	IC	Lab EPP	40 to 80	Arranged		C 5 to 10 days	Nil
Fundamentals of Virology (810)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 12	IC	Lab Lec O AV EPP	80	10/10/60	10/21/60	C 10 days	Nil

Key will be found on page 1670

CLINICAL PATHOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Laboratory Methods in the Diagnosis of Tuberculosis (855)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 12	IC	Lab Lec O AV FPP	80	10 31 60 1/30/61	11 11 60	C 10 days	Nil
Laboratory Methods in the Diagnosis of Rabies (826)	Communicable Disease Center Laboratory Branch, U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 15	IC	Lab Lec O AV FPP	40	11 28/60 1 3 61	12/ 2 60	C 5 days	Nil
Bacteriophage Typing of Staphylococci (856)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Lab M D s Lim 15	IC	Lab Lec O FPP	40	12 5 60	12/ 9 60	C 5 days	Nil
Laboratory Methods in Medical Mycology (815)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 22	IC	Lab Lec O AV EPP	160	1 9 61	2/3 61	C 20 days	Nil
Serologic Methods in Microbiology (941)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 10	IC	Lab Lec O AV FPP	120	1 23 61	2 10/61	C 15 days	Nil
Laboratory Methods in the Study of Pulmonary Mycoses (817)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 22	IC	Lab Lec O AV FPP	80	2 1 61	2 21 61	C 10 days	Nil
Laboratory Methods in Medical Bacteriology (838)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 20	IC	Lab Lec O AV FPP	120	2 27 61	17 61	C 15 days	Nil
Laboratory Diagnostic Methods in Veterinary Mycology (940)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 22	IC	Lab Lec O FPP	40	3 6 61	3 10 61	C 5 days	Nil
Lab Methods in the Diagnosis of Viral and Rickettsial Diseases (820)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 12	IC	Lab Lec O AV FPP	120	3 13 61	3 31/61	C 15 days	Nil
Special Problems in Medical Bacteriology (839)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 10	IC	Lab Lec O AV FPP	40	3 20 61	3 24/61	C 5 days	Nil
Laboratory Methods in Enteric Bacteriology (850)	Communicable Disease Center Laboratory Branch U S Public Health Service Atlanta 22 Ga	Lab Tech Open to M D s Lim 20	IC	Lab Lec O AV FPP	80	3 27 61	4/ 7/61	C 10 days	Nil
Modern Laboratory Procedures in Clinical Practice Their Use and Interpretation	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	Lab Sem Lec Pan O AV EPP	14	11/ 9/60	11/10/60	C 2 days	30
Medicine PM 22—Laboratory Methods in Blood Banks	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G Lim 6	II	Lab PD Clin C O AV	24	3/28/61	5/ 2 61	I 6 sessions 4 hr weekly Tuesdays	100
Laboratory Medicine	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 9	II	Lab Lec O AV	48	Arranged		I 24 sessions 2 hr Fridays	150
Clinical Chemistry—Recent Advances in the Field	Frank E Bunts Educational Institute 2020 E 93rd St Cleveland 6	G Lim 12	IC	PD LC Clin C Sem Lec Pan O	18	11/ 9/60	11/11/60	C 3 days	30

DERMATOLOGY

(See also Basic Sciences Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Advanced Seminars in Dermatology	University Extension—University of California Los Angeles University of California Medical Center Los Angeles course at University of California Conference Center Lake Arrowhead Calif	B	IC	Sem Lec Pan O AV	14½	7/61	Unknown	C 5 days	150
Dermatology	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	G	IC	Lec Pan O AV	14	10/14/60	10/15/60	C 2 days	Nil
Dermatology for General Practitioners	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	G	IC	LD Lec Pan O AV EPP	20	7/27/61	7/29/61	C 3 days	[illegible]

Clinical Dermatology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 5	PI	PD IC BR Clin C Lec O AV FPP	60	Arranged	2 wk later	10 days	75
Course II in Dermatology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 15	IC	PD IC BR Lec AV FPP	60	11/ 7/60 5/15/61	11/18/60	C 11 days	125
Dermatology (Medical Surgical Clinical Symposia)	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Lec Pan O AV	7	3/23/61	3/23/61	C 1 day	20
Dermatology and Syphilology 1	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	S Lim 4	IC	Lab PD LC BR Clin C Sem Lec AV FPP	1225 1400	10/ 3/60	9/30/61	C Unknown	800
Dermatology Clinical Conference	Wayne State University College of Medicine Department of Dermatology 1401 Rivard St Detroit course at Detroit Receiving Hospital Detroit	S Lim 10	II	PD IC Clin C O FPP	100	7/ 5/61	6/29/62	I 50 sessions 2 hr weekly Wednesdays	45
Dermatology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV	15	10/20/60	10/22/60	C 3 days	40
21 Dermatology and Syphilology (Designed for Pediatricians)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 30	IC	PD IC BR Clin C Surg Lec Pan O AV	35	10/10/60	10/14/60	C 5 days	100
23 Seminar in Dermatology and Syphilology (Designed for General Physicians)	New York University Post Graduate Medical School 550 First Ave New York	G Lim 30	IC	PD IC Clin C Sem Surg Lec Pan O AV FPP	35	2/13/61	2/17/61	C 5 days	100
24 Symposium on Dermatology and Syphilology (for Dermatologists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 30	IC	PD LC BR Clin C Sem Surg Lec Pan O AV FPP	35	5/15/61	5/17/61	C 5 days	125
Pediatric Dermatology	Skin and Cancer Hospital of Philadelphia 504 Pine St Philadelphia	B Lim 50	IC	Lec Pan O AV	40	11/14/60	11/18/60	C 5 days	100
Dermatopathology	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at M D Anderson Hospital and Tumor Institute Houston Texas	C Lim 20	II	Lec AV	15	9/14/60 Annually	12/21/60	I 15 sessions 1 hr weekly Wednesdays	30

ELECTROCARDIOGRAPHY

(See also Cardiovascular Disease)

Clinical Electrocardiography	University of Colorado School of Medicine 4200 E Ninth Ave Denver 20	G	II	Sem Lec	24	1/61	12 wk later	I 12 sessions 2 hr weekly Mondays	Unknown
Medicine 210—Clinical Electrocardiography	Yale University School of Medicine 333 Cedar St New Haven Conn	G Lim 30	II	Lec O AV FPP	12	9/20/60	12/ 6/60	I 12 sessions 1 hr weekly Tuesdays	50
Electrocardiography and Heart	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 30	IC	Lab PD IC BR Lec O AV FPP	70	10/ 3/60 5/15/61	10/14/60	C 11 days	150
One Week Advanced Course in Electrocardiography	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 30	IC	Lab Lec O AV FPP	35	6/19/61	6/23/61	C 5 days	100
Interpretation of Complex Arrhythmias	Cardiovascular Department Michael Reese Hospital 29th Street and Ellis Avenue Chicago	S	IC	Sem O AV FPP	30	12/ 5/60	12/ 9/60	C 5 days	100
Electrocardiographic Interpretation	Cardiographic Department Michael Reese Hospital 29th Street and Ellis Avenue Chicago	G	IC	Sem Lec O FPP	80	7/18/61	7/30/61	C 12 days	150
Electrocardiography	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	C	IC	Clin C Lec O AV	21	9/28/60	9/30/60	C 3 days	30
Interpretation of Electrocardiograms	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	HS(C)	Mailed tracings interpretations O	18	1/20/61	9/22/61	36 weekly lessons	40
Course in Clinical Electrocardiography	Maine Medical Center 22 Bramhall St Portland Maine	G	II	Lec Pan O AV FPP	15	1/11/61	3/15/61	I 10 sessions 1½ hr weekly Wednesdays	Nil
Practical Electrocardiography 2—Elementary Electrocardiographic Interpretation	Harvard Medical School 25 Shattuck St Boston course at Beth Israel Hospital Boston	G Lim 10	II	Lec Pan O AV FPP	30	10/ 5/60	12/14/60	I 10 sessions 3 hr weekly Wednesdays P M	100
Practical Electrocardiography 1—Elementary Electrocardiographic Interpretation	Harvard Medical School 25 Shattuck St Boston course at Beth Israel Hospital Boston	G Lim 10	IC	Lec Pan O AV FPP	30	11/ 7/60	11/11/60	C 5 days	100
Electrocardiogram Clinics 2—Applied Electrocardiography and Cardiology	Harvard Medical School 25 Shattuck St Boston course at Beth Israel Hospital Boston	G Lim 40	II	Clin C Sem Lec Pan O AV FPP	30	3/ 1/61	5/10/61	I 10 sessions 3 hr weekly Wednesdays P M	150

Key will be found on page 1670

ELECTROCARDIOGRAPHY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Electrocardiogram Clinics 1—Applied Electrocardiography and Cardiology	Harvard Medical School 25 Shattuck St Boston course at Beth Israel Hospital Boston	G Lim 40	IC	Clin C Sem Lec Pan O AV LPP	30	4/24/61	4/28/61	C 5 days	150
Clinical Electrocardiography	Harvard Medical School 25 Shattuck St Boston	S Lim 50	IC	Clin C, Sem Lec O AV	40	6/12/61	6/16/61	C 5 days	125
Electrocardiography I	Postgraduate Division Tufts University School of Medicine 171 Harrison Ave Boston 11 course at New England Center Hospital Boston 11	G Lim 25	IC	Clin C Lec, O AV	25	4/24/61	4/28/61	C, 5 days	60
Electrocardiography and Heart Disease	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor, Mich	G Lim 70	II	Sem Lec Pan O AV	38	9/27/60	2/7/61	I 2 hr weekly Tuesday evening	80
Electrocardiographic Diagnosis	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	G Lim 60	IC	Lab Lec O AV	35	3/27/61	4/1/61	C 5½ days	75
Electrocardiography	Highland Park General Hospital Highland Park Mich	S Lim 50	II	Clin C Lec O AV	28	10/15/60	3/15/61	I 28 sessions 1 hr weekly, Fridays	Unknown
Introduction to Electrocardiography for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV, EPP	30	1/3/61	1/7/61	C 5 days	60
Electrocardiology—Course 1	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IC	PD Sem Lec O AV LPP	12	2/6/61	2/7/61	C, 2 days	30
Advanced Clinical Electrocardiography	Seton Hall College of Medicine and Dentistry Medical Center 24 Baldwin Ave Jersey City 4 N J course at St Michael's Hospital, Newark, N J	G Lim 65	II	Sem O AV	22	10/60	4/61	I 22 sessions 1 hr weekly Wednesdays	40
Electrocardiography	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	PD Sem Lec Pan O AV EPP	21	11/16/60	11/18/60	C 3 days	45
Medicine PM 63A—Clinical Electrocardiography	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G	II	PD BR LEC O, AV EPP	36	9/20/60 2/7/61	1/31/61	I 18 sessions 2 hr weekly, Tuesdays	100
Medicine PM 40—Electrocardiography	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	IC	Lab PD Lec O AV	30	10/18/60 1/10/61	10/28/60	C 10 days	75
Medicine PM 43—Spatial Vectorcardiography and Vector Interpretation	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	IC	PD LEC, O AV	25	11/28/60	12/2/60	C 5 days	75
544 Electrocardiography	New York University Post Graduate Medical School 550 First Ave New York	G Lim 10	IC	PD Lec O AV	35	11/14/60 3/13/61	11/19/60	C 6 days	100
Electrocardiography	Rochester General Hospital 501 W Main St Rochester N Y	G Lim 50	II	Clin C Sem Lec Pan O AV	16	1/5/61	2/23/61	I 8 sessions 2 hr weekly, Thursdays	30
Initial and Advanced Courses in Electrocardiography	Duke University Medical Center Durham N C	G	IC	Lab Lec	15 to 18	1/61 6/61	Unknown	C, 3 days	100 includes maintenance
Electrocardiography	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G Lim 65	IC	Lab Lec Pan, O AV	32	5/1/61	5/5/61	C 5 days	75
Ballistocardiogram	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	S Lim 10	IC	PD Lec O		6/19/61	6/21/61	C 3 days	75
Advances in Electrocardiography	American College of Physicians 4200 Pine St Philadelphia 4 course at University of Tennessee Memphis Tenn	S	IC	PD Clin C Sem Lec Pan	40	Unknown	Unknown	C Unknown	60 members 80 non members
Electrocardiography	American College of Physicians 4200 Pine St Philadelphia 4 course at University of Utah College of Medicine Salt Lake City Utah	S	IC	PD Clin C Sem Lec Pan	10	11/7/60	11/11/60	C 5 days	60 members 80 non members

Electrocardiography	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at Citizens Memorial Hospital Victoria Texas	G	II	Lec O AV	8	3/ 7/61	3/28/61	I 4 sessions 2 hr weekly Tuesdays	Unknown
Vector Electrocardiography	University of Virginia School of Medicine Charlottesville Va	G	IC	Lab Clin C Surg Lec O AV EPP	18	1/26/61	1/28/61	C 3 days	10

ENDOCRINOLOGY

(See also Basic Sciences Gynecology Infertility Internal Medicine)

Clinical Endocrinology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 25	IC	Lab PD TC BR Lec AV EPP	35	6/ 5/61	6/ 9/61	C 5 days	100
Endocrinology (Medical Surgical Clinical Symposia)	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Lec Pan O AV	7	3/22/61	3/22/61	C 1 day	20
Endocrinology with Clinical Application	The University of Michigan Medical Center Department of Postgraduate Medicine 1010 University Hospital Ann Arbor Mich	S Lim 40	IC	PD Clin C Lec O AV	60	1/30/61	2/10/61	C 10 days	50
Endocrinology and Metabolism	The University of Michigan Medical Center Department of Postgraduate Medicine 1010 University Hospital Ann Arbor Mich	G Lim 60	IC	PD Clin C Lec O AV	30	4/17/61	4/21/61	C 5 days	50
General Endocrinology	Wayne State University College of Medicine 1401 Rivard Detroit 7	B	II	Lec O AV	32	2/61	6/61	I 16 sessions schedule unknown	45
Clinical Endocrinology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark N J	G Lim 45	II	Lec Pan O AV	15	2/ 1/61	4/12/61	I 10 sessions 1¼ hr weekly Wednesdays	50
Metabolic Endocrinology	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Kings County Hospital Brooklyn N Y	G Lim 25	II	TC Lec	15	10/60	12/60	I 10 sessions 1½ hr each days unknown	20
Endocrinology for the Generalist	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Jewish Hospital Brooklyn N Y	G Lim 20	II	Lec	10	4/61	5/61	I 10 sessions 1 hr each days unknown	20
Endocrinology	American College of Physicians 4200 Pine St Philadelphia 4 course at University of Virginia Charlottesville Va	S	IC	PD Clin C Sem Lec Pan	40	3/23/61	3/25/61	C 2 days	60 members 80 non members
12th Annual Post Graduate Assembly in Endocrinology	University of Wisconsin Madison Wis	B	IC	PD Clin C Lec Pan O AV		10/24/60	10/28/60	C 5 days	100

ENDOSCOPY

(See also Gynecology Otolaryngology)

Proctoscopy and Sigmoidoscopy	Cook County Graduate School of Medicine 707 S Wood St Chicago	G Lim 6	IC	Lab PD TC Lec AV TV EPP	13	9/26/60 10/24/60 1/30/61 3/20/61	10/ 1/60	C 5 days	100
Clinical Bronchoscopy	Cook County Graduate School of Medicine 707 S Wood St Chicago	G Lim 2	PI	Lab PD TC Surg Lec AV EPP	15	10/ 3/60 11/14/60 and monthly until July	10/ 7/60	5 days	100
Endoscopy	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston Texas	G Lim 1	II	Lab PD TC BR Sem Lec EPP	65	7/ 5/61	12/27/61	I 26 sessions 2½ hr weekly Wednesdays	100

EPHEBOLOGY

Adolescence	Tulane University School of Medicine 1430 Tulane Ave New Orleans	B Lim 50	IC	PD BR Clin C Lec Pan O AV EPP	28	2/ 8/61	2/11/61	C 3½ days	50
Adolescent Medicine I	Harvard Medical School 25 Shattuck St Boston course at Children's Hospital Medical Center Boston	G Lim 6	IC	PD LC Clin C Sem Lec O AV EPP	40 per wk	Arranged	Arranged	C Arranged	300

FRACTURES

(See also General Medicine Orthopedic Surgery)

Fractures	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	G	IC	Lec Pan O AV	20	11/ 3/60	11/ 5/60	C 3 days	35

Key will be found on page 1670

FRACTURES—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Fractures in General Practice	University of Florida College of Medicine Gainesville, Fla	G Lim 20	IC	PD, LC Sem Lec Pan O	10	9/22/60	9/23/60	C 2 days	25
Fractures in General Practice	Medical College of Georgia Augusta Ga	G Lim 20	IC	PD LC Clin C Sem Lec Pan	18	11/28/60	12/ 1/60	C 3 days	50
Course II—Clinical Fractures	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 3	PT	PD LC BR Clin C Surg EPP	6 per wk	Arranged	Friday following starting date	5 days	[illegible]0
Fractures	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 20	IC	PD Lec O AV	14	11/10/60	11/11/60	C 2 days	50
Sixth Annual Postgraduate Course in Fractures and Other Trauma	Cornell University Medical College 1300 York Ave New York 21	S	IC	Clin C Sem Lec Pan O	44	6/12/61	6/17/61	C 6 days	1[illegible]0
Fractures and Dislocations	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 20	IC	PD LC BR Clin C Sem Lec Pan O AV EPP	23	11/16/60	11/18/60	C 3 days	[illegible]
Fractures	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas	G	II	Lec, AV	8	5/ 2/61	5/23/61	I 4 sessions 2 hr weekly Tuesdays	20

GASTROENTEROLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Gastroscopy and Gastroenterology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim [illegible]	IC	Lab PD LC, Lec O AV EPP	40	9/12/60 11/ 7/60 2/ 7/61 4/17/61	9/23/60	C 12 days	200
Gastroenterology	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec, Pan O AV	7	4/27/61	4/27/61	C, 1 day	10
Clinical Traineeship in Gastroenterology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kansas	B Lim 2	PT	Lab LC, BR Clin C Sem Lec O, AV EPP	Arranged	Arranged	Unknown	Unknown	50 mo Kansas residents 100 mo nonresidents
Gastroenterology (Medical Surgical Clinical Symposia)	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Clin C Lec Pan O AV	7	3/21/61	3/21/61	C, 1 day	20
Gastroenterology	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IC	LC BR, Clin C, Sem, Lec Pan, O, AV	12	3/16/61	3/17/61	C 2 days	30
Gastroenterology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Harbor Mich	G Lim 50	IC	PD Lec Pan O, AV		2/27/61	3/ 3/61	C 5 days	50
Gastroenterology—Medical and Surgical Aspects	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2, N J course at All Souls Hospital, Morristown, N J	G Lim 50	II	Lec Pan, O AV	16½	9/22/60	12/ 8/60	I 11 sessions 1½ hr weekly, Thursdays	50
Medicine PM 70	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital, New York 67	G Lim 15	II	PD BR Sem Lec, O EPP	52½	9/20/60	1/17/61	I 15 sessions 3½ hr weekly Tuesdays	75
Medicine PM 73—Advanced Gastroenterology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G Lim 10	II	PD BR Sem, Lec O EPP	56	1/24/61	5/ 2/61	I 16 sessions 3½ hr weekly Tuesdays	75
Medicine PM 45—Gastroenterology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	IC	PD LC BR Lec, O AV	30	4/ 3/61	4/ 7/61	C 5 days	75
Advanced Gastroscopy—Instrumentation and Interpretation	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Division New York 29	S Lim 5	II	PD LC Clin C Lec EPP	20	Arranged		I 10 sessions 2 hr each days unknown	250
Gastroscopy	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital Division New York 29	S Lim [illegible]	II	PD LC Clin C Lec EPP	20	Arranged		I 8 sessions 2½ hr twice weekly Mondays Thursdays	250
Gastroenterology	New York Polyclinic Hospital [illegible] W 50th St New York 19	G Lim 10	IC	Lab PD LC BR Clin C Sem Lec O [illegible]	15	10/ 1/60 4/ 1/61	10/ /60	C [illegible] days	[illegible]0

Gastroenterology	Rochester General Hospital 501 W Main St Rochester N Y	G Lim 75	II	PD I C Clin C Lec Pan AV	10	1 / 1/60	12/ 8/60	I 2 sessions 5 hr twice Thursdays	15
Gastroenterology	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G	IC	PD LC Clin C Lec Pan O AV	21	2/13/61	2/15/61	C 3 days	15
Postgraduate Gastroenterology	American College of Gastroenterology 33 W 60th St New York 23 course at Bellevue Stratford Hotel Philadelphia 2	G	IC	Clin C Lec Pan	15	10/27/60	10/29/60	C 3 days	35 for members 50 for nonmembers
Gastroenterology	American College of Physicians 4200 Pine St Philadelphia 4 course at University of Pennsylvania Philadelphia	S	IC	PD Clin C Sem Lec Pan	40	5/61	5/61	C Unknown	60 members 80 non members
Diseases of the Digestive System	Marquette University School of Medicine 561 N 15th St Milwaukee course at Milwaukee County Hospital Wauwatosa Wis	G Lim 100	II	PD I C Lec O	12	4/ 6/61	4/27/61	I 4 sessions 3 hr weekly, Thursdays	30

GENERAL MEDICINE
(See also all other categories)

Medical Aspects of Modern Warfare	Surgeon General U S Air Force Headquarters USAF Washington 25 D C course at USAF Medical Service School Montgomery Ala	G Military M D only	IC	Lec Pan O AV	36	11/14/60 1/30/61 4/10/61	11/18/60	C 5 days	Nil
Postgraduate Circuit Courses—North Coast Counties	California Medical Association 2975 Wilshire Blvd Los Angeles course at various hospitals in Eureka Ukiah Napa Calif	G Lim 35	CO	I C Lec O AV	16	9/18/60	3/24/61	I 8 sessions 2 to 3 hr each schedule unknown	30
Postgraduate Circuit Courses—Sacramento Valley Counties	California Medical Association 2975 Wilshire Blvd Los Angeles course at various hospitals in Redding Marysville Chico Auburn Calif	G Lim 35	CO	I C Lec O AV	21	9/18/60	3/21/61	I 8 sessions 1 afternoon 2 evenings schedule unknown	30
Southern Counties Regional Postgraduate Institute	California Medical Association 2975 Wilshire Blvd Los Angeles course at El Mirador Hotel Palm Springs Calif	G	IC	Clin C Lec Pan O AV EPP	12	2/ 2/61	2/ 3/61	C 2 days	15
West Coast Counties Regional Postgraduate Institute	California Medical Association 2975 Wilshire Blvd Los Angeles course at Del Monte Lodge Pebble Beach Calif	G	IC	Lec Pan O AV	12	3/ 2/61	3/ 3/61	C 2 days	15
North Coast Counties Regional Postgraduate Institute Psychological Factors in Medical Practice	California Medical Association 2975 Wilshire Blvd Los Angeles Location of course not selected	B	IC	Sem Lec Pan O	14	4/61	Unknown	C 2 days	15
Sacramento Valley Counties Regional Postgraduate Institute	California Medical Association 2975 Wilshire Blvd Los Angeles course at Tahoe Tavern Tahoe City Calif	B	IC	Clin C Sem Lec Pan O AV	12	6/29/61	6/30/61	C 2 days	15
San Joaquin Valley Counties Regional Postgraduate Institute	California Medical Association 2975 Wilshire Blvd Los Angeles course at Ahwahnee Hotel Yosemite Calif	G	IC	Clin C Sem Lec Pan O AV	12	4/13/61	4/14/61	C 2 days	15
Fourteenth Postgraduate Assembly	San Diego County General Hospital North end of Front Street San Diego 3 Calif	S Lim 100	IC	BR Sem Lec AV	16	11/ 9/60	11/10/60	C 2 days	Nil
Psychologic Problems of Medical Practice	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco course at University of California Extension Center San Francisco	G	IC	Clin C Sem Lec Pan O AV	21	11/11/60	11/13/60	C 3 days	5
Control of the Mind The Individual and Civilization	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	G	IC	Lec Pan O AV	18	3/25/61	3/27/61	C 3 days	Unknown
Saint John's Hospital Postgraduate Assembly	Saint John's Hospital 1328 22nd St Santa Monica Calif	B Lim 600	IC	Clin C Sem Lec Pan O	28	9/ 8/60	9/10/60	C 3 days	Nil
Stockton Post Graduate Study Club	San Joaquin Company Medical Society P O Box 230 Stockton Calif course at College of the Pacific Stockton Calif	G	II	Lec O AV	12	9/ 8/60	11/10/60	I 8 sessions 1½ hr weekly Thursdays	10
7th Annual General Practice Review	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	G	IC	Lec Pan O AV	48	1/ 9/61	1/14/61	C 6 days	10 per day or 50 full course plus 10
Summer School of Alcohol Studies	Summer School of Alcohol Studies Yale University 52 Hillhouse Ave Yale Station New Haven Conn	G and non M D personnel Lim 275	IC	PD Sem Lec Pan O AV	74	6/25/61	7/20/61	C 22 days	275

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GENERAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Medicine for Today—Traumatic Surgery and Orthopedics Obstetrical Emergencies Endocrinology, Psychiatry and Allergy	Illinois Academy of General Practice 14 E Jackson Blvd Suite 1512 Chicago 4 course at Aurora, Chicago (North), Chicago (South) Elmhurst Kankakee Oak Park Rockford Waukegan Ottawa, Alton Centralia Effingham Moline, Peoria	G	CC	Lec, O AV	24	10/ 3/60	4/21/61	I schedule unknown	50 for I A G P members 90 for nonmembers
American Academy of General Practice Postgraduate Courses—Cardiovascular Disease and Emotional Problems	Illinois Academy of General Practice 14 E Jackson Blvd Chicago 4 course at Oak Park Hospital Oak Park Ill	G	II	Unknown	30	9/60 3/61	11/60	I Unknown	40 members 50 nonmembers
Arthritis and Rheumatism	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	PD Sem Lec Pan O AV	10	9/23/60	9/24/60	C 1½ days	20
Refresher Course for the General Physician	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	PD Clin C Sem Lec Pan, O AV	25	2/21/61	2/24/61	C, 4 days	40
Neurology Neurosurgery Orthopedics Conference—Symposium on Painful Conditions	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	PD Clin C, Lec Pan O AV	12	4/ 4/61	4/ 5/61	C 2 days	20
Infectious Diseases	American Academy of General Practice Volker Boulevard at Brookside Kansas City 12 Mo course at University of Kansas School of Medicine Kansas City 12 Kan	B	IC	Lec Pan O AV	7	9/23/60	9/23/60	C 1 day	Nil
Kansas Circuit Course	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City, Kansas course at Riley County Hospital, Manhattan Kan St Joseph Hospital Concordia Kan St Elizabeth's Mercy Hospital, Hutchinson, Kan Location not selected Colby Kan Hotel Osage Arkansas City, Kan St Catherine Hospital Garden City Kan Newman Memorial Hospital Emporia Kan	B	CC	PD Clin C, Lec Pan O AV	33	12/ 6/60 12/ 6/60 12/ 7/60 12/ 7/60 12/ 8/60 12/ 8/60 12/ 9/60 12/ 9/60	4/25/61 4/25/61 4/26/61 4/26/61 4/27/61 4/27/61 4/28/61 4/28/61	I 6 sessions 5½ hr weekly	30
Medicine and the Family Physician	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	G	II	PD, Lec Pan O, AV	24	11/10/60	4/20/61	I 6 sessions 4 hr monthly, Thursdays	25
General Medicine and Surgery	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan course at Southeast Kansas Tuberculosis Hospital Chanute, Kan	G	II	Lec, O, AV	6	11/15/60	4/18/61	I 6 sessions 1 hr monthly, Tuesdays	15
Medical Surgical Clinical Symposia	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD LC, Lec, Pan, O, AV	35	3/20/61	3/24/61	C 5 days	80
Fifth Annual Fall Clinical Conference—Lexington Clinic	Lexington Clinic 1221 S Broadway, Lexington, Ky	G	IC	Clin C Pan	7	10/27/60 Annually	10/27/60	C 1 day	Nil
Fifth Annual Fall Clinical Conference—Symposia on Gynecology Virus Diseases Convulsions Common Medical Problems	Lexington Clinic 1221 S Broadway Lexington Ky	G	IC	PD Clin C Sem Lec Pan O AV	7	10/27/60	10/27/60	C 1 day	Nil
John N Norton Memorial Infirmary Medical Seminar	Robert Lich Jr M D Norton Infirmary 801 Heyburn Bldg Louisville Ky	G	IC	Sem	8	12/14/60 Annually	12/14/60	C 1 day	Nil
Review of Selected Medical Subjects	Louisiana State University School of Medicine 1542 Tulane Ave New Orleans course at Confederate Memorial Hospital Shreveport La	G Lim 150	II	PD LC Clin C, Sem Lec, O, AV EPP	42	9/60	5/61	I Unknown	Unknown
Therapeutic Pharmacology of the Newer Drugs	Central Maine General Hospital Lewiston Maine	G Lim 100	II	PD Sem, Lec, O AV	18	10/ 6/60	11/10/60	I 6 sessions 3 hr weekly Thursdays	30
Course in Respiratory and Circulatory Resuscitation	Maine Medical Center 22 Bramhall St Portland Maine	G Lim 40	II	PD, Lec, O AV EPP	15	3/22/61	5/24/51	I 10 sessions 1½ hr weekly Wednesdays	Nil
Symposium on the Ankle and Foot	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	G Lim 100	IC	PD LC BR Clin C Sem Lec Pan O AV EPP	12	11/ 4/60	11/ 5/60	C 2 days	50
Symposium on the Hand	Harvard Medical School Shattuck St Boston	G Lim 100	IC	PD LC BR Clin C Sem Lec Pan O AV EPP	12	Spring 1961	2 days later	C - days	50

New Bedford Course in General Medicine	Postgraduate Medical Institute 22 Fenway Boston 15 course at St Luke's Hospital New Bedford Mass	G	II	Pan AV	20	9/ 8/60	12/14/60	I 10 sessions 2 hr weekly Wednesdays	60
Boston Fall Course in General Medicine	Postgraduate Medical Institute 22 Fenway Boston 15 course at Lemuel Shattuck Hospital Boston 30	G	II	PD Pan AV	20	10/ 5/60 2/15/61	12/ 7/60	I 8 sessions 2½ hr weekly Wednesdays	50
Connecticut Valley Course in General Medicine	Postgraduate Medical Institute 22 Fenway Boston course at Holyoke Soldiers Home Holyoke Mass Cooley Dickinson Hospital Northampton Mass 5 sessions at each hospital	G	II	Pan AV	20	10/16/60	12/ 9/60	I 10 sessions 2 hr weekly Fridays	50
Trauma for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV	7	3/18/61	3/18/61	C 1 day	10
Clinical Conferences Including all Clinical Fields	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	C Lim 60	II	PD Clin C Lec Pan O AV	95	10/ 5/60	2/22/61	I 19 sessions 5 hr weekly Wednesdays	65
Rheumatology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	C Lim 60	IC	Lab PD Clin C Lec O AV	18	4/24/61	4/26/61	C 3 days	40
Recent Advances in Therapeutics	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 60	IC	Lab PD Clin C Lec O AV	34	4/24/61	4/28/61	C 5 days	50
Psychotherapy in General Practice	Wayne State University College of Medicine 1401 Rivard Detroit 7	G Lim 15	II	LC Clin C Sem Lec	27	9/28/60 2/ 8/61	2/ 1/61	I 18 sessions 1½ hr weekly Wednesdays	33 75
Circuit Courses	University of Mississippi School of Medicine University Medical Center Jackson Miss course at North Mississippi Community Hospital Tupelo Miss Greenwood Leflore Hospital Greenwood Miss Memorial Hospital Gulfport Miss Methodist Hospital Hattiesburg Miss Matty Hersee Hospital Meridian Miss University Medical Center Jackson Miss	G	CO	Sem Lec Pan O AV	15	Unknown	Unknown	I 1 day weekly	Nil
Clinical Traineeship (Clinical Field by Arrangement)	The University of Mississippi School of Medicine University Medical Center Jackson Miss	G Lim 4	PT	PD LC BR Clin C Sem Lec O AV TV	Unknown	Arranged	Unknown	Unknown	Nil
General Medicine and Surgery	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan course at Northwest Missouri Chapter Missouri Academy of General Practice (Moila Temple) St Joseph Mo	G	II	Lec O AV	9	9/20/60	5/16/61	I 9 sessions 1 hr monthly Tuesdays	Nil
Visiting Chief Program	Atlantic City Hospital 20 S Ohio Ave Atlantic City N J	B Lim 50	II	PD LC BR Clin C Lec O AV	480	Continuous		I 2 hr daily 5 p m 5 days wk	Nil
Medical Management in Geriatrics	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J	G Lim 45	II	Lec O AV	9	Unknown	Unknown	I 6 sessions schedule unknown	35
Selected Topics of Interest to the Practitioner	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Elizabeth General Hospital Elizabeth N J	G Lim 45	II	Lec Pan O AV	15	9/21/60	6/21/61	I 10 sessions 1½ hr monthly Wednesdays	50
Recent Advances in Clinical Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Monmouth Medical Center Long Branch N J	G Lim 45	II	Lec O AV	15	10/ 4/60	11/ 9/60	I 10 sessions 1½ hr every other Tuesday	Unknown
Recent Advances in Medicine and Surgery	Seton Hall College of Medicine and Dentistry 31 Clinton St Newark 2 N J course at Mountainside Hospital Montclair N J	G Lim 45	II	Lec O AV	22½	10/ 5/60	1/25/61	I 15 sessions 1½ hr weekly Wednesdays	50

Key will be found on page 1670

GENERAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Case Oriented Clinical Discussion	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St, Newark 2 N J course at Saint Elizabeth Hospital Elizabeth N J	G Lim 45	II	Clin C Lec O AV	16	10/ 7/60	2/ 3/61	I 16 sessions 1 hr weekly Fridays	50
Seminar in Arthritis and Related Diseases	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J	G Lim 60	IC	Sem Lec Pan O AV	12	11/ 4/60	11/ 5/60	C 1½ days	15
One Day Postgraduate Seminar on Selected Topics in Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at St Francis Hospital, Trenton, N J	G Lim 45	IC	Lec Pan O	1	11/16/60	11/16/60	C 1 day	25
Recent Advances in Medicine and Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at St Barnabas Medical Center Newark 2 N J	G Lim 45	II	Lec Pan O AV	15	1/11/61	3/15/61	I 10 sessions 1½ hr weekly Wednesdays	50
Recent Advances in Clinical Medicine II	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark N J course at Fitkin Memorial Hospital Neptune N J	G Lim 45	II	Lec O AV	15	2/21/61	4/ 4/61	I 10 sessions 1½ hr every other Tuesday	50
Ruidoso Summer Clinics	New Mexico Academy of General Practice Dr Randall W Briggs 406 N Pennsylvania Roswell, N Mex course at Knob Hill School Ruidoso N Mex	G	IC	Lec Pan, O AV	14	7/18/60	7/21/60	C 4 days	25 or 20 in advance
Recent Advances in Clinical Practice	University of Buffalo School of Medicine 3435 Main St, Buffalo 14 N Y	G	IC	PD LC BR Sem Lec Pan O AV EPP	39	9/12/60	9/17/60	C 6 days	75
The State Hospital and the Practitioner of Medicine	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	Sem Lec Pan O AV EPP	5	10/13/60	10/13/60	C 1 day	10
Arthritis	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	PD LC Sem Lec, Pan O AV EPP	14	4/ 5/61	4/ 6/61	C 2 days	30
Medicine PM 81—Arthritis	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Hospital for Joint Diseases New York 35	G	IC	Lab LC Lec O, AV EPP	20	4/20/61	4/23/61	C 4 days	100
Postgraduate Week	The New York Academy of Medicine 2 E 103rd St New York 29	G	IC	Lec Pan, O AV	18	10/21/60	10/28/60	C, 5 days	Nil
Diagnosis and Treatment of Medical and Pediatric Renal Diseases	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital New York	B Lim 80	II	Lab PD LC Sem Lec O EPP	22	11/ 9/60	1/21/61	I 11 sessions 2 hr each days unknown	300
Comprehensive Course in Medicine	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 120	IC	Lab PD LC BR Clin C Sem Lec O AV TV EPP	1260	9/60	6/61	C 180 days	800
Evening Courses for the General Practitioner	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 20	II	Lec O EPP	12	10/ 1/60 4/ 1/61	11/28/60	I 8 sessions 1½ hr weekly	50
Survey Course for Foreign Medical School Graduates	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 125	IC	Clin C Sem Lec Pan O AV	Unknown	2/ 6/61	3/17/61	C 20 days	75
717—General Medicine	New York University Post Graduate Medical School 550 First Ave New York	G	II	Clin C Lec, O AV	70	9/20/60	4/18/61	I 28 sessions 2½ hr weekly Tuesdays	275
811—Arthritis and Related Disorders for General Physicians	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	IC	Lab PD Lec AV	35	5/15/61	5/18/61	C 4 days	85
Buncombe County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C course at Memorial Mission Hospital Asheville N C	G	II	Lec Pan O AV	18	10/ 4/60	11/ 8/60	I 6 sessions 3 hr weekly Tuesdays	25
Burke County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C course at [illegible] Hospital Morganton N C	G	II	Lec Pan O AV	18	10/ /60	11/ 9/60	I 6 sessions 3 hr weekly Wednesdays	25

University of North Carolina School of Medicine Symposium	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C	G	IC	PD BR Clin C Lec Pan O AV EPP	12	11/17/60	11/18/60	C 2 days	Nil
Lenoir Greene Jones Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C Location of course not selected	G	II	Lec Pan O AV	18	1/61	2/61	I 6 sessions 3 hr each days unknown	25
First District Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C course at Edenton Restaurant Edenton N C	G	II	Lec Pan O AV	18	1/11/61	2/22/61	I 6 sessions 3 hr weekly Wednesdays	25
Robeson County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C Location of course not selected	G	II	PD Clin C Lec Pan O AV EPP	18	3/61	4/61	I 6 sessions 3 hr each days unknown	25
Catawba Iredell Alexander Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine P O Box 1020 Chapel Hill N C Location of course not selected	G	II	Lec Pan O AV	18	3/61	4/61	I 6 sessions 3 hr each days unknown	25
Refresher Course	School of Medicine University of North Dakota Grand Forks N D	G	IC	Lab Clin C Lec	8	11/17/60	11/17/60	C 1 day	Unknown
General Practice	Frank E Bunts Educational Institute 2020 E 93rd St Cleveland	G Lim 125	IC	PD Clin C Lec Pan O AV	12	2/ 8/61	2/ 9/61	C 2 days	20
Selected Topics in Medicine	School of Medicine Western Reserve University 2109 Adelbert Rd Cleveland 6	G Lim 85	II	PD Clin C Sem Lec Pan O AV	30	9/14/60	11/16/60	I 10 sessions 3 hr weekly Wednesdays	35
Problems of the Aged	St Vincent Hospital Department of General Practice 232 W 25th St Erie Pa	G Lim 40	II	Lab PD LC BR Clin C Lec Pan O AV EPP	28	10/12/60	11/23/60	I 7 sessions 4 hr weekly Wednesdays	35
Psychotherapy in General Practice	Hahnemann Medical College 235 N 15th St Philadelphia	G Lim 15	II	Sem Lec O AV	12	10/20/60	12/ 8/60	I unknown	15
1960-61 Postgraduate Course in Psychosomatic Medicine	Temple University Medical Center 3400 N Broad St Philadelphia 40	B Lim 20	II	Lab PD LC Clin C Sem Lec Pan O EPP	80	10/ 5/60	2/22/61	I 20 sessions 4 hr weekly Wednesdays	40
Recent Advances in Medicine	Temple University Medical Center Broad and Ontario Streets Philadelphia 40	G Lim 50	II	PD LC BR Clin C Sem Lec Pan O	32	10/19/60	12/ 7/60	I 8 sessions 4 hr each Wednesdays	50
Clinical Medicine	Medical Society State of Pennsylvania State Street Harrisburg Pa course at U S Veterans Hospital Pittsburgh	G	II	PD LC BR Clin C Sem Surg Lec Pan O AV EPP	60	3/30/61	6/ 1/61	I 10 sessions 6 hr weekly Thursdays	65
Founders Day Postgraduate Seminar	Medical College of South Carolina 16 Lucas St Charleston S C	G	IC	PD Sem Lec Pan AV	Unknown	11/16/60	11/17/60	C 2 days	Nil
Postgraduate Reviews	Vanderbilt University School of Medicine and Hospital 21st Avenue South Nashville 5 Tenn	G	II	PD LC Clin C Lec Pan O	Unknown	Unknown	Unknown	I 7 hr Thursdays episodically	15
Hill Country Medical Seminars	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at Villa Camille Hunt Texas	G	IC	Lec O AV	12	7/24/61	7/26/61	C 3 days	50
Hill Country Medical Seminars	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at Villa Camille Hunt Texas	G	IC	Lec O AV	12	8/ 7/61	8/ 9/61	C 3 days	50
Ninth Postgraduate Conference in Medicine and Surgery	Scott and White Memorial Hospital and Scott Sherwood and Brindley Foundation Temple Division University of Texas Postgraduate School of Medicine 213 W Avenue G Temple Texas	G	IC	Lab PD LC BR Clin C Sem Surg Lec Pan O AV EPP	20	3/ 6/61	3/ 8/61	C 3 days	25
Seminar on Infections	University of Virginia School of Medicine Charlottesville Va	G	IC	Clin C Sem Lec Pan O AV	12	9/30/60	10/ 1/60	C 2 days	Nil
Midsummer Clinic Day	Washington Academy of General Practice 216 W 37th St Vancouver Wash course at University of Washington Medical School Seattle Wash	G	IC	Lec Pan O	6	8/ 5/61	8/ 5/61	C 1 day	Nil
Newer Concepts—Medicine Surgery Obstetrics and Gynecology	Mt Sinai Hospital 918 N 12th St Milwaukee Wis	C Lim 150	II	Sem Lec Pan O AV	12	10/12/60	Unknown	I 2 sessions 6 hr weekly 2 Wednesdays	25

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GYNECOLOGY

(See also Anatomy Malignant Disease, Obstetrics and Gynecology, Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Fall Symposia in Obstetrics and Gynecology	Continuing Education in Medicine and The Health Sciences University of California San Francisco Second and Parnassus San Francisco	G	IC	Sem, Lec Pan, O AV	18	9/15/60	9/17/60	C, 3 days	50
Course II in Gynecology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 18	IC	PD LC BR Clin C, Surg Lec, AV, TV EPP	90	9/12/60 10/30/60 2/20/61 4/24/61 6/12/61	9/23/60	C 11 days	150
Gynecology 3	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	S Lim 50	IC	PD LC Clin C Sem Lec, Pan, O AV, EPP	78	9/12/60	9/23/60	C 10 days	175
Gynecology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV	15	5/ 8/61	5/10/61	C 3 days	40
Office Gynecology	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Jewish Hospital Brooklyn N Y	G Lim 25	II	Lec	10	10/60	11/60	I 10 sessions 1 hr each, days unknown	20
Culdoscopy	New York Polyclinic Hospital 345 W 50th St New York 19	S Lim 10	IC	PD Lec, O EPP	6	Unknown	Unknown	C 3 days	100
564—Gynecological Cytology (For Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 6	II	Lab Sem Lec O AV, EPP	32	9/27/60 4/11/61	11/17/60	I 16 sessions 1 and 3 hr weekly Tuesdays, Thursdays	100
560—Diagnosis and Therapy of Malignant Neoplasms of the Female Genital Tract	New York University Post Graduate Medical School 550 First Ave New York	S Lim 8	IC	Lab PD LC Clin C Sem Surg Lec, O AV, EPP	35	10/ 3/60	10/ 7/60	C 5 days	150
563—Gynecological Endocrinology	New York University Post Graduate Medical School 550 First Ave New York	G Lim 30	IC	Lab, PD, LC Clin C Sem, Lec AV, EPP	35	10/17/60 4/17/61	10/21/60	C 5 days	140
562—Culdoscopy	New York University Post Graduate Medical School 550 First Ave New York	G Lim 4	II	PD LC Surg Lec O, AV, EPP	6	11/14/60 4/24/61	11/18/60	I 3 sessions 2 hr thrice weekly Mondays, Wednesdays, Fridays	55
Carcinoma of the Uterus	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at Wisconsin Center Building, Madison 6 Wis	S	IC	PD LC, Clin C Sem, Lec, Pan O AV EPP	17½	10/27/60	10/29/60	C 2½ days	50
HEMATOLOGY (See also Clinical Pathology)									
Diagnosis and Treatment of Anemia	University Extension—University of California Los Angeles University of California Medical Center Los Angeles	B	IC	Sem Lec Pan, O AV	12	12/ 9/60	12/10/60	C 2 days	40
Clinical Hematology	Office of Postgraduate Medical Education, University of Colorado Medical Center 4200 E Ninth Ave Denver 20	S Lim 12	IC	Lab, Lec, EPP	48	6/61	6/61	C, 6 days	100
Hematology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 30	IC	Lab PD, LC BR, Clin C, Lec O AV	30	6/ 5/61	6/ 9/61	C 5 days	100
Treatment of Common Disorders of the Blood	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec, Pan O, AV	7	4/26/61	4/26/61	C 1 day	10
Hematology—II	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	HS (C)	AV	15	8/30/60 1/26/61	4/25/61	9 monthly lessons	45
Clinical Traineeship in Hematology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 1	PT	Lab BR Clin C Sem Lec O AV EPP	120	11/ 1/60 2/ 1/61 3/ 1/61	11/30/60	30 days	50 mo Kansas residents 100 mo non residents
Hematology—I	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	HS (C)	AV	15	9/ 6/60 2/ 2/61	5/ 2/61	9 monthly lessons	15
Hematology	Postgraduate Division Tufts University School of Medicine 171 Harrison Av Boston 11 course at New England Center Hospital Boston 11	G Lim [illegible]	IC	PD Clin C Sem Lec Pan O AV	15	3/23/61	3/25/61	C 3 days	30

Diseases of the Blood	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 40	IC	Lab PD Clin C Lec O AV	30	4/ 3/61	4/ 7/61	C 5 days	50
Blood as Functional Tissue	Wayne State University College of Medicine 1401 Rivard Detroit 7	B	II	Sem Lec O	32	2/61	6/61	I 16 sessions schedule known	45
Hematology	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	C	IC	Lab Clin C Sem Lec Pan O AV	Unknown	Unknown	Unknown	C 1 day	15
Medicine I M 60—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G Lim 20	II	Lab PD LC BR Lec O	72	9/21/60	1/25/61	I 18 sessions 4 hr weekly Wednesdays	150
Medicine PM 20—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	II	Lab PD LC Lec O AV	24	11/ 1/60	12/20/60	I 8 sessions 3 hr weekly Tuesdays	100
Medicine PM [illegible]—Advanced Hematology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G Lim 20	II	Lec PD LC BR Lec O	37½	2/ 1/61	5/24/61	I 15 sessions 2½ hr weekly Wednesdays	150
Medicine PM 21—Laboratory Methods in Hematology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	C Lim 6	IC	Lab Clin C EPP	64	2/13/61	3/ 9/61	O 16 days	300
Hematology	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G Lim 8	II	Lab Clin C Sem Lec, O	16	Arranged		I 8 sessions 2 hr each days unknown	100
17—Hematology	New York University Post Graduate Medical School [illegible]0 First Ave New York	G Lim 20	IC	PD LC Lec Pan O AV	35	11/ 7/60 5/ 8/61	11/11/60	C 5 days	90
13—Hematology	New York University Post Graduate Medical School [illegible]0 First Ave New York	G Lim 20	II	PD LC Lec Pan O FPP	32	3/ 7/61	4/27/61	I 16 sessions 2 hr twice weekly Tuesdays Thursdays	55
Postgraduate Course in Hematology	American College of Physicians 4200 Pine St Philadelphia 4 course at The Ohio State University Columbus 10 Ohio	B Lim 75	IC	Lab PD LC Lec Pan O AV EPP	40	9/19/60	9/24/60	C 5 days	Unknown
Hematology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	Specialty Board Candidates Lim 50	IC	Lab Lec Pan O AV	Unknown	Unknown		C 3 days	75
Practical Pediatric Hematology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	G Lim 50	IC	PD LC BR Clin C Sem Lec Pan O AV	Unknown	6/ 6/61	6/10/61	C 5 days	75
Clinical Hematology	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	S Lim 20	IC	Lab PD BR Clin C Sem Lec Pan O AV FPP	23	9/14/60	9/16/60	C 3 days	50
Morphological Hematology	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G Lim 30	II	Lab Lec O AV	12	9/ 7/60	11/23/60	I 12 sessions 1 hr weekly Wednesdays	25
Anemia Workshop	University of Washington School of Medicine Seattle 5	S	IC	Lab Sem Lec Pan O AV FPP	Unknown	9/15/60	9/17/60	C 3 days	Unknown
Blood Disorders in Pediatrics	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at Wisconsin Center Building Madison 6 Wis	S	IC	PD Clin C Sem Lec Pan O AV FPP	17½	4/13/61	4/15/61	C 2½ days	60

INFERTILITY
(See also Basic Sciences)

Infertility and Endocrinology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 40	IC	Lab PD Lec O	14	3/ 9/61	3/10/61	C 2 days	30
Infertility	Joint Committee on Postgraduate Education 1313 Bedford Ave Brooklyn N Y course at Cumberland Hospital Brooklyn N Y	G Lim 20	II	Lec	16	4/61	5/61	I 8 sessions 2 hr each days unknown	30
Physiology of Reproduction	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 20	II	Sem Lec	12	Arranged		I 6 sessions 2 hr each days unknown	75

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INFERTILITY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Symposium on Fertility and Infertility	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg., Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G	IC	Lec Pan AV	16	1/61	Unknown	C 3 days	Unknown

INTERNAL MEDICINE

(See also Basic Sciences, Cardiovascular Disease Chest Diseases Gastroenterology General Medicine Hematology Malignant Disease Psychiatry)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Low Back Pain	University Extension—University of California Los Angeles University of California Medical Center Los Angeles	B	IC	Sem Lec Pan O, AV	12	5/12/61	5/13/61	C 2 days	40
Advanced Seminars in Internal Medicine	University Extension—University of California Los Angeles University of California Medical Center Los Angeles course at University of California Conference Center Lake Arrowhead Calif	B	IC	Sem Lec Pan O AV	18	7/61	Unknown	C 4 days	150
Dynamics of Endocrine and Metabolic Diseases	Institute for Metabolic Research 2701 14th Ave Oakland 6, Calif course at Highland Alameda County Hospital Oakland 6 Calif	S Lim 60	IC	PD Sem Lec Pan O AV	24	2/ 6/61	2/ 8/61	C 3 days	50
Present Concepts in Internal Medicine	Letterman General Hospital San Francisco	G Lim 150	IC	PD LC Clin C Lec Pan	40	11/14/60	11/18/60	C 5 days	Nil
Internal Medicine	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	G	IC	Lec Pan O AV	35	9/28/60	10/ 2/60	C 5 days	90 (or 20 per day)
Internal Medicine	American College of Physicians 4200 Pine St Philadelphia 4 course at McGill University Montreal Quebec Canada	S	IC	PD Clin C Sem Lec Pan	40	Unknown	Unknown	C Unknown	60 members 80 non members
Psychiatry for the Internist	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	S Lim 25	IC	PD LC BR Clin C Sem Lec Pan AV EPP	40	6/19/61	6/23/61	C 5 days	Unknown
Diagnosis and Management of Diseases of the Kidney	Yale University School of Medicine 333 Cedar St New Haven Conn	G Lim 100	II	Clin C Lec AV	16	2/ 1/61	3/22/61	I 8 sessions 2 hr weekly Wednesdays	40
Diabetes Seminar	State Board of Health and Florida Diabetes Association P O Box 210 Jacksonville Fla course at Soreno Hotel St Petersburg Fla	G Lim 100	IC	PD LC Clin C Sem Lec Pan O AV	16	10/27/60	10/28/60	C 2 days	25
Workshop on Diabetes	Medical College of Georgia Augusta Ga	G Lim 20	IC	PD LC, Clin C Sem, Lec Pan	18	12/ 6/60	12/ 8/60	C 3 days	50
Internal Medicine for the Internist—Part I	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Candidates Lim 200	IC	Lec AV	60	9/12/60 9/11/61	9/17/60	C 6 days	125
Two Week Basic Course in Internal Medicine	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 30	IC	PD LC BR Clin C Lec O, AV, TV, EPP	80	10/17/60 5/ 1/61	10/28/60	C 11 days	150
Internal Medicine for the Internist—Part II	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S candidates Lim 40	IC	PD LC BR, Sem Lec O AV, EPP	48	12/ 5/60 3/13/61	12/10/60	C, 6 days	150
Recent Advances in Physical Diagnosis	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	PD, Lec, O, AV	7	1/12/61	1/12/61	C, 1 day	10
Weight Reduction and General Dietary Therapy	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec Pan O, AV	7	1/26/61	1/26/61	C 1 day	10
Internal Medicine	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Clin C Lec, Pan O AV	28	11/14/60	11/17/60	C, 4 days	60
Hypertension	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Lec, Pan O AV	14	2/13/61	2/14/61	C, 2 days	35
Diabetes	Central Maine General Hospital Lewiston Maine	C Lim 100	II	PD Clin C Lec O AV	18	4/61	5/61	I 6 sessions 3 hr weekly Thursdays	Unknown
Topics in Clinical Medicine	Johns Hopkins Medical School and Hospital Broadway Baltimore	S Lim 150	IC	PD LC Clin C Sem Lec Pan O AV	38	2nd Wk in 5/61		C 5½ days	125

Postgraduate Course in Internal Medicine	Harvard Medical School Shattuck St Boston course at Massachusetts General Hospital Boston	S Lim 50	IC	LC Clin C Lec O	200	Unknown		C 36 days	400
Diabetes Mellitus in Relation to General Medicine	Harvard Medical School 25 Shattuck St Boston course at New England Deaconess Hospital Boston	G Lim 60	IC	PD IC BR Clin C Sem Lec Pan O AV	21	10/ 3/60	10/ 5/60	C 3 days	30
Recent Advances in Internal Medicine	Harvard Medical School 25 Shattuck St Boston course at Peter Bent Brigham Hospital Boston	S Lim 125	IC	Sem Lec O AV	33	6/ 5/61	6/10/61	C 6 days	150
Internal Medicine 3	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	B Lim 50	IC	PD LC Clin C Sem Lec Pan O AV	210	6/12/61	7/21/61	C 35 days	400
Review of Recent Advances in Internal Medicine	Postgraduate Division Tufts University School of Medicine 171 Harrison Ave Boston 11 course at New England Center Hospital Boston 11	G Lim 100	IC	PD LC Sem, Lec Pan O AV EPP	40	10/10/60	10/15/60	C 5½ days	75
Clinical Postgraduate Program—Mexico City	University Extension—University of California Los Angeles University of California Medical Center Los Angeles course at The National School of Medicine Mexico City	B	IC	Sem Lec Pan O AV	18	2/12/61	2/22/61	C 11 days	100
Clinical Internal Medicine	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 60	II	PD Surg Pan O AV	66	10/ 6/60	3/ 2/61	I 19 sessions 3½ hr weekly Thursdays	65
Selected Clinical Topics	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 70	II	Lec Pan O AV	24	2/14/61	5/ 2/61	I 12 sessions 2 hr weekly Tuesdays	50
Recent Developments in Pharmacology and Therapeutics	Wayne State University College of Medicine 1401 Rivard Detroit 7	B	II	Sem Lec O	16	9/60	2/61	I 16 sessions 1 hr weekly days unknown	22 50
Post Graduate Seminars	Highland Park General Hospital Highland Park Mich	S Lim 50	II	PD BR Clin C Sem Lec O AV EPP	100	Unknown		I 52 sessions 1½ 2 hr weekly	Unknown
Internal Medicine for Internists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	B	IC	Lec Pan O AV	18	5/25/61	5/27/61	C 3 days	40
Recent Advances in Internal Medicine and Therapeutics	Middlesex General Hospital 180 Somerset St New Brunswick N J	G Lim 80	II	Sem Lec O AV	64	9/28/60 9/61	5/31/61	I 32 sessions 2 hr weekly Wednesdays	100 or for interns resid 25
Recent Advances in Internal Medicine and Endocrinology	Seton Hall College of Medicine and Dentistry Medical Center 74 Baldwin Ave Jersey City 4 N J course at St Michael's Hospital Newark N J	G Lim 60	II	PD LC BR Clin C, Lec O AV	20	10/60	3/61	I 10 sessions 2 hr alternate Wednesdays	10
Metabolic Emergencies	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Holy Name Hospital Teaneck N J	G Lim 15	II	Lec O AV	9	2/ 7/61	3/14/61	I 6 sessions 1½ hr weekly, Tuesdays	35
Recent Advances in Internal Medicine	Lovelace Foundation 1800 Gibson Blvd S E Albuquerque N Mex course at Bataan Memorial Methodist Hospital Albuquerque N Mex	G Lim 10	IC	Lab PD BR Clin C Sem Lec Pan O EPP	30	1/ 9/61	1/13/61	C 5 days	60
Selected Subjects in Therapeutics	Booth Memorial Hospital 56-45 Main St Flushing 55 N Y	B Lim 25	II	Lec	15	3/16/61	5/18/61	I 10 sessions 1½ hr weekly Thursdays	Unknown
Medicine PM 4	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G	II	PD BR Sem Lec O AV EPP	72	9/20/60 2/ 7/61	1/31/61	I 18 sessions 4 hr weekly Tuesdays	150 per section
Medicine I M 1—Chemotherapy of Infections and Parasitic Diseases	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	II	Lab PD LC Lec Pan O AV	9	10/18/60 3/ 7/61	11/ 3/60	I 6 sessions 1½ hr twice weekly Tuesdays, Thursdays	50

Key will be found on page 1670

INTERNAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Medicine PM 50—Diseases of the Liver	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32 course at Mount Sinai Hospital New York 29	G	IC	PD, BR, Lec, O, AV, EPP	30	10/21/60	10/28/60	C 5 days	100
Recent Advances in Internal Medicine	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Kings County Hospital Brooklyn N Y	G Lim 30	II	Lec, Pan	15	10/60	12/60	I 10 sessions 1½ hr each, days unknown	20
Diabetes Mellitus	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Jewish Chronic Disease Hospital, Brooklyn N Y	G Lim 20	II	PD, Lec	8	4/61	5/61	I 8 sessions 1 hr each, days unknown	20
Modern Therapeutics in Internal Medicine	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Coney Island Hospital, Brooklyn N Y	G Lim 30	II	Lec	15	4/61	6/61	I 10 sessions 1½ hr each days unknown	30
Diabetes and Basic Metabolic Problems	American Diabetes Association, Inc 1 E 45th St New York 17 course at Louisiana State University School of Medicine Auditorium New Orleans	G Lim 250	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	20	1/18/61	1/20/61	C 3 days	40 members, 75 non members
Review of Current Progress in Internal Medicine	Maimonides Hospital of Brooklyn 4802 Tenth Ave Brooklyn 19, N Y	B Lim 100	II	PD, LC, BR, Clin C Sem Lec, Pan, O AV, EPP	40	1/ 3/61	3/ 9/61	I 20 sessions 2 hr twice weekly Tuesdays, Thursdays	50
5412—Arthritis and Related Disorders For the Experienced Clinician and Research Worker	New York University Post Graduate Medical School 550 First Ave New York	G	IC	Lab, PD, Lec, Pan, AV	35	3/13/61	3/17/61	C, 5 days	100
Recent Advances in Medicine	Rochester General Hospital 501 W Main St Rochester N Y	G Lim 75	IC	Clin C, Lec, Pan, AV	6	3/30/61	One day	C 1 day	10
Recent Advances in the Diagnosis and Treatment of Endocrine and Metabolic Disorders	University of Rochester Medical Center 260 Crittenden Blvd Rochester N Y course at Rochester Regional Hospital Council Rochester, N Y	G Lim 25	IC	BR, Lec, Pan, O, AV	16	11/17/60	11/19/60	C 2½ days	40
Seventh Annual Seminar—Collagen and Rheumatic Diseases	Huron Road Hospital 13951 Terrace Rd Cleveland 12	G	IC	Sem, Pan	14	5/ 5/61	5/ 6/61	C 2 days	25
Selected Topics in Internal Medicine	School of Medicine Western Reserve University 2109 Adelbert Rd Cleveland 6	G Lim 85	II	PD, Clin C Sem, Lec, Pan O, AV	28	Spring 1961		I 8 sessions 3½ hr weekly Wednesdays	35
Fifth Annual Sessions on Rheumatic Diseases	Ohio State University Columbus 10 Ohio	G Lim 200	IC	Lec, Pan, O	8	10/16/60	10/16/60	C, 1 day	10
Selected Topics in Internal Medicine	American College of Physicians 4200 Pine St Philadelphia 4 course at The University of Oklahoma School of Medicine and University Hospitals Oklahoma City Okla	S	IC	PD, Clin C, Sem, Lec, Pan	40	2/20/61	2/24/61	C 5 days	60 members 80 non members
Problems of Growth and Aging	American College of Physicians 4200 Pine St Philadelphia 4 course at Lankenau Medical Building Philadelphia Pa	S	IC	PD, Clin C, Sem, Lec Pan	40	4/12/61	4/15/61	C 4 days	60 members 80 non members
Present Concepts of Carbohydrate Metabolism—Diabetes	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	G Lim 50	IC	Sem, Lec, Pan, O		2/20/61	2/22/61	C 3 days	75
Postgraduate Education	Tennessee State Medical Association 112 Louise Ave Nashville Tenn course at Vanderbilt University School of Medicine Nashville Tenn University of Tennessee Memphis Tenn	G	CC	Lec Pan	All day	Fall 1900	One day	1 day	10
Diabetes	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas	G	IC	Lec AV	6	2/12/61	2/12/61	C 1 day	Unknown
Recent Advances in Drug Therapy	American College of Physicians 4200 Pine St Philadelphia 4 course at University of Washington School of Medicine Seattle	S	IC	PD Clin C Sem Lec Pan	40	1/ 9/61	1/13/61	C 5 days	60 members 80 non members
Arthritis and Its Control	University of Washington School of Medicine Seattle	B	IC	Sem Lec Pan O AV	Unknown	10/26/60	10/27/60	C 2 days	Unknown

Current Views in Medical Practice—Medicine and Its Specialties	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at University Hospitals Madison 6 Wis	G	II	PD LC Clin C Sem Lec Pan O AV EPP	16	1/19/61	2/ 9/61	I 4 sessions 4 hr weekly Thursdays	25
Current Problems in Internal Medicine	Marquette University School of Medicine 561 N 15th St Milwaukee course at Milwaukee County Hospital Wauwatosa	G Lim 100	II	PD I C Lec O	12	3/ 1/61	3/22/61	I 4 sessions 3 hr weekly Wednesdays	30

MALIGNANT DISEASE

(See also Gynecology Pathology Pediatrics Radiology Surgery)

Cancer Seminar	State Board of Health and American Cancer Society P O Box 210 Jacksonville Fla course at Cherry Plaza Hotel Orlando Fla	G Lim 500	IC	I C Clin C Sem Lec Pan O AV	20	11/16/60	11/18/60	C 3 days	Nil
Cancer Symposium	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec Pan O AV	7	3/29/61	3/29/61	C 1 day	Nil
Recent Advances in Diagnosis and Therapeutic Techniques in Cancer	Tulane University School of Medicine 1430 Tulane Ave New Orleans	G Lim 40	IC	Lab PD LC Clin C Lec Pan TV EPP	20	3/ 2/61	3/ 4/61	C 2½ days	25
Cancer Teaching Clinic	Westfield State Sanatorium Westfield Mass	G	IC	PD Clin C Sem Lec Pan O AV	2	11/16/60 4/12/61	11/16/60	C 1 day	Nil
Cancer Detection for General Physicians	Continuation Medical Education 1312 Mayo Memorial University of Minnesota Minneapolis 14 course at Cancer Detection Center Minneapolis	G Lim 2	IC	PD EPP	12	Arranged	2 days later	C 2 days	25 (5 from applicant 20 from American Cancer Society)
Cancer Seminar	The University of Mississippi School of Medicine University Medical Center Jackson Miss	G Lim 150	IC	PD Clin C Sem Lec Pan O AV TV	6	12/ 8/60	12/ 8/60	C 1 day	Nil
Newer Concepts in the Treatment of Cancer	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at United Hospital of Newark—Presbyterian Hospital Unit Newark N J	G Lim 45	II	Lec O AV	10	2/ 7/61	4/11/61	I 10 sessions 1 hr weekly Tuesdays	50
Medicine I M 72—Neoplastic diseases	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G	II	PD BR Clin C Sem Lec O AV	140	9/21/60 2/ 1/61	1/25/61	I 20 sessions 7 hr weekly Wednesdays	150
Medicine PM 1—Basic Research in Neoplastic Diseases and Its Application to Clinical Cancer	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Francis Delafield Hospital New York 32	G Lim 50	IC	Sem Lec Pan O AV	35	11/28/60	12/ 3/60	C 5 days	100
Diagnosis and Management of Early Cancer	Sloan Kettering Institute 410 E 68th St New York course at Memorial Center for Cancer and Allied Diseases New York	G Lim 20	IC	Lab PD I C Clin C	25	9/26/60 April or May 1961	9/29/60	C 4 days	40
Course in Cancer Chemotherapy	Sloan Kettering Institute 410 E 68th St New York course at Memorial Center for Cancer and Allied Diseases New York	S Lim 25	IC	PD LC BR Clin C Sem Lec Pan O AV	60	10/17/60	10/28/60	C 10 days	50
Cancer and the Internist—1960 Concepts	American College of Physicians 4200 Pine St Philadelphia 4 course at Memorial Sloan Kettering Institute for Cancer Research New York	S	IC	PD Clin C Sem Lec Pan	40	10/10/60	10/14/60	C 5 days	60 members 80 non members
Malignant Tumors of the Female Pelvis	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston Texas	G	IC	Lec Pan AV	12	10/21/60	10/22/60	C 2 days	Unknown
Pediatric Oncology	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G Lim 200	IC	Lec AV	Unknown	11/ 4/60	11/ 5/60	C 2 days	Unknown
Nucleic Acid Proteins and Cancer (15th Annual Symposium)	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G	IC	Lec Pan O AV	Unknown	2/23/61	2/25/61	C 3 days	Unknown

Key will be found on page 1670

MALIGNANT DISEASES—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Advances in the Chemotherapy of Malignant Diseases	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at Wisconsin Center Building Madison 6 Wis	S	IC	PD LC Clin C Sem Surg Lec Pan O AV EPP	17½	8/25/60	8/27/60	C 2½ days	50

NEUROLOGY

(See also Basic Sciences Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Seminar in Medicine	University of Florida College of Medicine Gainesville Fla	B	IC	Clin C Sem Lec Pan O	15	Unknown	Unknown	C 2½ days	25
The Neuromuscular Diseases of Children with Special Emphasis on Cerebral Palsy	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 30	IC	Lab PD LC Clin C Sem Lec O AV EPP	80	6/12/61	6/23/61	C 11 days	250
Twelfth Annual Western Institute on Epilepsy	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Lec Pan O AV	11	9/16/60	9/17/60	C 2 days	25
Neurological Medicine	Harvard Medical School 25 Shattuck St Boston course at Boston City Hospital Boston	S Lim 20	IC	PD LC BR Clin C Sem Lec O EPP	11	6/5/61	6/10/61	C 5 days	150
Neurology	Postgraduate Division Tufts University School of Medicine 171 Harrison Ave Boston 11 course at New England Center Hospital Boston 11	G Lim 30	IC	PD Lec O AV	15	5/4/61	5/6/61	C 3 days	30
Clinical Neurology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 60	IC	PD Clin C, Lec O AV	11	3/13/61	3/14/61	C 2 days	30
Clinical Neurosurgery	Wayne State University College of Medicine 1401 Rivard, Detroit course at Grace Central Hospital Detroit	S	II	Lab PD LC Clin C Sem Lec O OV	36	9/60	6/61	I 36 sessions schedule unknown	45
Clinical Neurology and Neuroroentgenology	Wayne State University College of Medicine 1401 Rivard St Detroit course at Detroit Receiving Hospital and Lafayette Clinic Detroit	G Lim 5	II	PD LC BR Clin C, Sem Lec EPP	30	7/1/61 Annually	6/30/62	I 15 sessions schedule unknown	45
Neurology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14	G	IC	Lec Pan O, AV	18	2/13/61	2/17/61	C 5 days	40
Neuropathology, Including Allied Basic Sciences C N S Anatomy Physiology and Pathology	Eastern Psychiatric Research Association c/o Director Kings Park State Hospital Kings Park, N Y	S Lim 8	II	Lab Lec AV EPP	30	10/5/60	12/21/60	I 12 sessions 2½ hr weekly	Nil
Neurology PM 33—Clinical Electroencephalography	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	II	Lec, O AV, EPP	45	9/22/60	1/5/61	I 15 sessions 3 hr weekly Thursdays	100
Neurology PM 30—Clinical Neurology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	IO	PD LC Sem Lec O AV	30	3/27/61	3/31/61	C 5 days	75
Neurology PM 1—Pediatric Neurology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32	S Lim 50	IO	PD Sem Lec O AV	35	5/22/61	5/26/61	C 5 days	100
Advanced Functional Neuroanatomy	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St, New York	G Lim 25	II	Lec	22	Arranged		I 11 sessions 2 hr each days unknown	100
611 Electroencephalography	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 6	IO	Lab	Arranged	Arranged		C Arranged	375
603 For The General Practitioner Acute Problems of Central Nervous System	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	IO	PD LC BR, Clin C Lec AV	35	10/10/60 4/24/61 6/19/61	10/14/60	C 5 days	125
602 Diagnosis and Treatment of Peripheral Nerve Injuries	New York University Post Graduate Medical School 550 First Ave New York	G Lim 8	IC	Lab PD, Surg Lec, EPP	14	1/5/61	1/6/61	C 2 days	50
Review of Neurology	Coldwater Memorial Hospital and Manhattan State Hospital Welfare Island New York and Wards Island New York	S Lim 24	II	Lab PD Lec	100	9/14/60	12/9/60	I 19 sessions 2 to 3 hr daily except Thursdays and Saturdays	175
Neurology	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G	IO	PD LC Clin C Lec Pan O AV	21	10/17/60	10/19/60	C 3 days	45

Electroencephalography	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	G	IC	Sem Lec O AV EPP		3/1 /61	3/17/61	C 3 days	7
Neurology	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 20	IC	PD Clin C Sem Lec Pan O AV	23	4/26/61	4/28/61	C 3 days	[illegible]

NEUROLOGY AND PSYCHIATRY

Fourteenth Connecticut Postgraduate Seminar in Psychiatry and Neurology	Yale University School of Medicine 333 Cedar St New Haven Conn	S	II	Lec O AV	146	9/21/60	5/31/61	I 73 sessions 2 hr twice weekly Mondays Wednesdays	Nil
Post Graduate Course in Psychiatry and Neurology	Lafayette Clinic 951 E Lafayette Detroit	S	PT	PD Clin C Lec Pan O	120	9/29/60	5/26/61	70 days	Nil
Neurology and Psychiatry in General Practice	University of Nebraska College of Medicine 42nd and Dewey Omaha 5 course at Nebraska Psychiatric Institute Omaha 5	G	IC	PD Clin C Sem Lec Pan O AV TV	6	11/17/60	11/17/60	C 1 day	15
Psychiatry PM 1	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S	IC	Lab PD Lec O AV EPP	350	10/ 3/60	12/ 9/60	C 50 days	300
PM 1 Psychiatry	New York State Psychiatric Institute 722 W 168th St New York 32 course at Columbia University College of Physicians and Surgeons New York 32	S Lim 60	IC	Lab PD LC Clin C Lec AV	350	10/ 3/60	12/ 9/60	C 50 days	300
C13 Neurology and Psychiatry	New York University Post Graduate Medical School 550 First Ave New York 16	G	IC	PD LC Lec	420	9/12/60	12/ 2/60	C 60 days	325
816 Basic Psychiatry and Neurology	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Lec	24	9/30/60 2/10/61 (course 816)	1/20/61	I 16 sessions 1½ hr weekly Fridays	75

OBSTETRICS

(See also Obstetrics and Gynecology Pathology)

Course I—Obstetrics	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 14	IC	PD LC BR Clin C Surg Lec O AV EPP	75	10/ 3/60 11/28/60 2/ 6/61 4/10/61 5/15/61	10/14/60	C 11 days	150
Obstetrics	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Clin C Lec Pan O AV	21	11/ 7/60	11/ 9/60	C 3 days	45
Obstetrics for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV	18	10/ 3/60	10/ 5/60	C 3 days	40
Obstetrics	University of Nebraska College of Medicine 42nd and Dewey Omaha 5 course at Lincoln General Hospital Lincoln Neb	G	IC	LC Clin C Sem Lec Pan O AV	6	3/30/61	3/30/61	C, 1 day	15
Three Afternoon Seminars in Obstetrics	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Margaret Hague Maternity Hospital Jersey City 4 N J	G Lim 45	IC	PD Sem Lec Pan O AV	9	1/18/61	2/ 1/61	I 3 sessions 3 hr weekly Wednesdays	30
Operative Obstetrics (Manikin)	New York Polyclinic Hospital 345 W 50th St New York	G Lim 10	IC	Clin C Sem Lec O EPP	16	10/ 1/60 1/ 1/61	10/31/60	I 16 sessions 2 hr twice weekly Wednesdays Fridays	150

OBSTETRICS AND GYNECOLOGY

(See also Anatomy Malignant Disease Pathology)

Obstetrics and Gynecology	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	B	IC	Sem Lec O AV	12	7/10/61	7/12/61	C 3 days	35
Postgraduate Course in Radiation Physics for Active or Junior Fellows	The American College of Obstetricians and Gynecologists 9 W Monroe St Chicago 3 course at Americana Hotel Bal Harbour Fla	S Lim 35 Members	IC	Clin C Sem Lec Pan O AV	12	4/21/61	4/23/61	C 3 days	35

Key will be found on page 1670

OBSTETRICS AND GYNECOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Course in Biostatistics for Active and Junior Fellows	The American College of Obstetricians and Gynecologists 79 W Monroe St Chicago course at Americana Hotel Bal Harbour Fla	S Lim 35 Members	IC	Clin C Sem Lec, Pan O AV	12	4/21/61	4/23/61	C 3 days	35
Postgraduate Course in Genetics and Human Reproduction for Active or Junior Fellows	The American College of Obstetricians and Gynecologists 79 W Monroe St Chicago course at Americana Hotel Bal Harbour Fla	S Lim 35 Members	IC	Clin C Sem Lec Pan O AV	12	4/21/61	4/23/61	C 3 days	35
Postgraduate Course on Steroid Metabolism for Active or Junior Fellows	The American College of Obstetricians and Gynecologists 79 W Monroe St Chicago course at Americana Hotel Bal Harbour Fla	S Lim 35 Members	IC	Clin C Sem Lec Pan O AV	12	4/21/61	4/23/61	C 3 days	35
Postgraduate Course in Electrolyte and Fluid Balance for Active or Junior Fellows	The American College of Obstetricians and Gynecologists 79 W Monroe St Chicago course at Americana Hotel Bal Harbour Fla	S Lim 35 Members	IC	Clin C Sem Lec Pan O AV	12	4/21/61	4/23/61	C 3 days	35
Obstetrics and Gynecology	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	Lec Pan O AV	11	3/ 8/61	3/ 9/61	C 1½ days	20
Obstetrics and Gynecology	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	Lec Pan O AV	6	1/11/61	1/11/61	C 1 day	15
Pathology of Obstetrics and Gynecology	Harvard Medical School 25 Shattuck St Boston	S Lim 12	II	Lab Lec AV	100	1/ 5/61	5/18/61	I 20 sessions 5 hr weekly Thursdays	200
Obstetrics and Gynecology	Harvard Medical School 25 Shattuck St Boston course at Free Hospital for Women Brookline Mass Boston Lying-in Hospital Boston	B Lim 50	IC	Lab PD LC, BR Clin C Sem Lec Pan O AV EPP	75	3/20/61	3/31/61	C 11 days	200
Obstetrics and Gynecology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 60	IC	PD Clin C Lec O, AV	18	1/25/61	1/27/61	C 3 days	30
Obstetrics and Gynecology	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IC	LC BR, Clin C Sem Lec Pan O, AV	12	1/19/61	1/20/61	C 2 days	30
Obstetrics and Gynecology Traineeship for the General Physician	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G Lim 6	PT	PD LC BR Clin C Sem Surg Lec Pan O AV EPP	45	6/19/61	6/24/61	5½ days	75
Selected Topics in Obstetrics and Gynecology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Paterson General Hospital Paterson N J	G Lim 15	II	Lec O AV	16½	9/16/60	11/25/60	I 11 sessions 1½ Hr weekly Fridays	50
Obstetrics and Gynecology	University of Buffalo School of Medicine 3435 Main St Buffalo	G Lim 16	IC	Sem Lec Pan O AV LPP	14	11/30/60	12/ 1/60	C 2 days	30
Gynecology and Obstetrics Including Manikin Obstetrics and Operative Gynecology (Cadaver)	New York Polyclinic Hospital 345 W 50th St New York	G Lim 10	IC	Lab PD LC BR Clin C Sem Lec O LPP	120	10/ 1/60 4/ 1/61	10/31/60	C 20 days	250
Recent Advance in Obstetrics and Gynecology	State University of New York Downstate Medical Center 450 Clarkson Ave Brooklyn 3 N Y course at Maimonides Hospital of Brooklyn Brooklyn 19 New York	G Lim 100	II	PD LC BR Clin C Lec O AV	24	10/ 4/60	12/20/60	I 2 hr weekly Tuesdays	35
Obstetrics and Gynecology	Rochester Regional Hospital Council 164 East Ave Rochester 4 N Y course at University of Rochester Medical Center Rochester 20 N Y	G Lim 25	IC	LC Sem Pan O AV LPP		6/22/61	6/24/61	C 3 days	45
Obstetrics and Gynecology	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G Lim 65	IC	PD LC Clin C Lec Pan O AV	22	11/10/60	11/11/60	C 3 days	15
Obstetrics and Gynecology	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 20	IC	PD LC BR Clin C Lec Pan O AV	23	10/26/60	10/28/60	C 3 days	[illegible]
Armed Forces Seminar in Obstetrics and Gynecology	Brooke General Hospital Brooke Army Medical Center Fort Sam	S Lim 200	IC	Sem Lec Pan O AV	[illegible]	10/17/60	10/20/60	C 4 days	Nil

Obstetrics and Gynecology	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at Turner Home El Paso Texas	G Lim 60	IC	Lec Pan O AV	7	1/22/61	1/22/61	C 1 day	10

OCCUPATIONAL MEDICINE

Workshop in Industrial Medicine	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco course at University of California Extension Center San Francisco	B	IC	Sem Lec O AV	18	9/12/60	9/14/60	C 3 days	Unknown
School Health	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	G	IC	Sem Lec Pan O AV	7	10/ 6/60	10/ 6/60	C 1 day	Nil
Industrial Medicine	Postgraduate Committee University of Maryland School of Medicine 22 W Lombard St Baltimore	G Lim 100	II	Lec Pan O	14	10/ 6/60	10/13/60	I 2 sessions 7 hr weekly Thursdays	20
Industrial Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J	G Lim 30	II	Lec O AV	Unknown	Unknown	Unknown	I schedule unknown	25
Infant and Preschool In Service Training Course	Bureau of Child Health 125 Worth St New York course at Kips Bay Health Center New York	C Lim 6	IC	PD LC Clin C Sem Lec Pan AV EPP	24	Arranged	Unknown	C 4 days	15
Infant and Preschool In Service Training Course	Bureau of Child Health 125 Worth St New York course at Kips Bay Health Center New York	G	IC	LC Clin C Sem Lec Pan AV EPP	60	9/60 5/61	9/60	C 20 days	15 per session
Pre Service Training Course for School Physicians	Bureau of School Health Department of Health 125 Worth St New York course at Kips Bay Health Center Department of Health New York	G	IC	I C Sem Lec Pan AV TV EPP	90	9/60 4/61	10/60	C 30 days	Trainee is paid 15 per session
Occupational Medicine 02	Columbia University School of Public Health and Administrative Medicine 600 W 168th St New York 32	G Lim 6	II	Clin C, Sem Lec	24	1/30/61	3/25/61	I 16 sessions 1½ hr twice weekly Mondays Thursdays	80
Institute for Physicians in Industry	Columbia University School of Public Health 600 W 168th St New York 32	S Lim 16	IC	Clin C Lec	48	2/10/61 2/62	2/14/61	C 4 days	144
Occupational Medicine 03—Industrial Medical Organization	Columbia University School of Public Health and Administrative Medicine 600 W 168th St New York 32	G	II	Lec O AV	18	3/27/61	6/20/61	I Unknown arrangement	40
180 Industrial Hygiene	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians Lim 30	II	Lab Lec	Unknown	9/60		I Unknown	100
181 Occupational Medicine for Physicians	New York University Post Graduate Medical School 550 First Ave New York	G Lim 30	IC	Sem Lec Pan AV	280	9/12/60	11/ 4/60	C 40 days	375 plus 25 Field Trip Fee
182 Occupational Medicine for Physicians (Part Time Course)	New York University Post Graduate Medical School 550 First Ave New York	G Lim 30	II	Lec Pan AV	90	9/15/60	5/11/61	I 30 sessions 3 hr weekly Thursdays	300
183 Introduction to Radiological Health	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians Lim 35	IC	Lab Lec AV	70	10/10/60	10/21/60	C 10 days	100
184 Medical Aspects of Compensation	New York University Post Graduate Medical School 550 First Ave New York	G Lim 100	IC	Sem Lec Pan AV	35	10/17/60	10/21/60	C 5 days	60
183 L Radiological Health Laboratory	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians Lim 10	IC	Lab Lec AV	Unknown	10/24/60	11/ 4/60	C Unknown	100
1811 Radiochemical Analysis	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians	IC	Lab Lec AV	70	11/ 7/60	11/18/60	C 10 days	100
1810 Air Pollution	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians	IC	Lab Lec AV	70	11/28/60	12/ 9/60	C 10 days	100
180 L Industrial Hygiene Laboratory	New York University Post Graduate Medical School 550 First Ave New York	G and non physicians Lim 10	II	Lab	Unknown	2/61		I Unknown	100

Key will be found on page 1670

OCCUPATIONAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
4815 Medical and Public Health Control of Ionizing Radiation	New York University Post Graduate Medical School 550 First Ave, New York	G and non physicians	IC	Lab Lec, AV	70	3/ 6/61	3/17/61	C, 10 days	110
1813 Radiation Hygiene Measurements	New York University Post Graduate Medical School 550 First Ave, New York	G and non physicians Lim 16	IC	Lab, Lec, AV	110	4/17/61	5/12/61	C, 20 days	200
Postgraduate Institute for Physicians on Medical Aspects of High School Athletics	Ohio State Medical Association 79 E State St Columbus 15 Ohio course at College of Medicine The Ohio State University Columbus 10 Ohio	G Lim 150	IC	Sem, Lec, Pan, EPP	12	8/31/60	9/ 1/60	C, 12 days	25
7th Annual Postgraduate Course in Aviation Medicine	The Ohio State University College of Medicine Columbus 10 Ohio	B Lim 60	IC	Sem, Lec Pan, O, AV, TV EPP	40	9/12/60	9/16/60	C 5 days	75

OPHTHALMOLOGY

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Basic Sciences in Ophthalmology	University Extension—University of California Los Angeles University of California Medical Center, Los Angeles	S	II	Clin C, Lec, O, AV	45	9/60	6/61	I, schedule unknown	45
Advances in Surgical Anatomy Normal Anatomy and Histology of the Eye	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	S	IC	Lec Pan O, AV	18	9/22/60	9/24/60	C 3 days	50
Ophthalmology	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	G	IC	Sem, Lec Pan O, AV	18	12/ 1/60	12/ 3/60	C 3 days	50
Symposium on Eye Problems in Children	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco course at Children s Hospital, San Francisco	G	IC	Lec Pan O AV	7	1/14/61	1/14/61	C 1 day	12 50
Ophthalmology	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	S	IC	Sem Lec, Pan O, AV	20	7/61	7/61	C 4 days	50
Postgraduate Series in Ophthalmology	Yale University School of Medicine 333 Cedar St New Haven Conn	S	II	Lec	13½	10/28/60	2/10/61	I 9 sessions 1½ hr alternate Fridays	25
Techniques in Ophthalmic Surgery	Department of Ophthalmology, Emory University School of Medicine 69 Butler St S E Atlanta 3, Ga course at Grady Memorial Hospital Atlanta 3 Ga	S	IC	Clin C Sem, Lec, Pan AV	16	12/ 1/60	12/ 2/60	C 2 days	Unknown
Clinical Ophthalmology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 4	PT	PD LC, BR Clin C Surg, O, AV, EPP	50	Arranged	2 wk later	10 days	50
Extraocular Muscles I—Diagnosis & Treatment of Strabismus	Northwestern University Medical School 303 E Chicago Ave Chicago 11	S Ophth Lim 5	IC	PD LC, Sem, Lec	24	9/12/60	9/23/60	C 10 days	100
Extraocular Muscles II—Diagnosis and Treatment of Strabismus	Northwestern University Medical School 303 E Chicago Ave Chicago 11	S Ophth Lim 5	II	PD LC BR Sem, Lec	200	Unknown		I, Unknown	150
Clinical Traineeship in Ophthalmology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S Lim 1	PT	Lab, PD, BR Clin C Sem, Lec, O, AV EPP	Unknown	Arranged	Unknown	Unknown	50 mo Kansas residents 100 mo nonresidents
Cataract Surgery	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S Lim 10	IC	Lec O, AV	14	12/ 9/60	12/10/60	C 2 days	50
Ophthalmology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S	IC	Lec Pan O, AV	17	4/12/61	4/14/61	C 3 days	10
Lancaster Courses in Ophthalmology	Ophthalmological Study Council York Hill Sullivan Harbor Maine course at Colby College Waterville Maine	B	IC	Lab Clin C Sem Lec Pan O EPP	446	6/17/61	9/ 2/61	C 66 days	380
Ophthalmology	Harvard Medical School 25 Shattuck St Boston course at Harvard Medical School Massachusetts Eye and Ear Infirmary Boston	S Lim 30	IC	Lab LC Lec AV	726	9/26/60	3/11/61	C Unknown	67
151 Clinical N[illegible] Ophthalmology	Massachusetts Eye and Ear Infirmary	[illegible]	IC	[illegible] LC Lec O	30	5/61	[illegible]/61	C 6 days	[illegible]

Ophthalmology	The University of Michigan Medical Center Department of Postgraduate Medicine 1[illegible]10 University Hospital Ann Arbor Mich	S Lim 1[illegible]0	IC	Lec O AV	18	4/[illegible]4/61	4/[illegible]6/61	C 3 days	[illegible]0
Ophthalmology for General Physicians (Refraction)	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	C Lim	IC	PD LC Lec Pan O AV EPP	18	11/14/60	11/16/60	C 3 days	40
Ophthalmology for General Physicians (Refraction)	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14	G Lim [illegible]	IC	PD LC Lec Pan O AV EPP	18	11/16/60	11/18/60	C 3 days	40
Ophthalmology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	S	IC	Lec Pan O AV	18	[illegible]/ 1/61	5/ 3/61	C 3 days	40
Home Study Course in Ophthalmology	American Academy of Ophthalmology and Otolaryngology 1[illegible] Second St S W Rochester Minn	S	HS(C)	Assigned reading		9/ 1/60 9/ 1/61	6/30/61	Monthly assignments and exams by mail	20
Gonioscopy and Glaucoma	Brooklyn Eye and Ear Infirmary 29 Greene Ave Brooklyn N Y	S Lim 6	IC	PD Lec O EPP	18	Unknown		C 3 days	[illegible]0
Keratoplasty Course	The Eye Bank for Sight Restoration Inc 210 E 6[illegible]th St New York 21	S	IC	Lab PD LC BR Lec EPP	30	Spring 1961 Annually		C [illegible] days	1[illegible]0
Ophthalmology PM 31 Glaucoma	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	II	PD Lec O AV EPP	9	10/ 4/60	10/21/60	I 6 sessions 1½ hr twice weekly Tuesdays Fridays	50
Ophthalmology PM 60 Elementary Ophthalmoscopy	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	B	II	PD Lec O AV	16	10/2[illegible]/60	12/[illegible]0/60	I 8 sessions 2 hr weekly Tuesdays	30
Ophthalmology PM 60—Elementary Ophthalmoscopy	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	G Lim 20	II	PD LC BR Lec AV	16	10/2[illegible]/60	12/20/60	I 8 sessions 2 hr weekly Tuesdays	30
Ophthalmology PM [illegible]—Opthalmoscopy for General Practitioners and Pediatricians	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G Lim 12	II	Lab PD Clin C EPP	12	11/ 3/60	12/ 1/60	I 8 sessions 1½ hr twice weekly Tuesdays Thursdays	Unknown
Ophthalmology PM 33—The Use of the Schepens Ophthalmoscope	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 8	II	Lab PD Sem EPP	12	3/ 7/61	3/23/61	I 6 sessions 2 hr twice weekly Tuesdays Thursdays	[illegible]0
Ophthalmology PM 30—Histopathology of the Eye	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 10	II	Lab PD Clin C Lec O AV EPP	16	4/ [illegible]/61	4/28/61	I 8 sessions 2 hr twice weekly Wednesdays Fridays	100
Amblyopia	Institute of Ophthalmology 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 3[illegible]	II	PD LC Lec O AV EPP	18	Winter 1961		I 6 sessions 3 hr thrice weekly Mondays Wednesdays Fridays	100
Plastic Eye Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 10	II	PD LC Surg Lec O AV EPP	42	9/12/60	9/29/60	I Unknown	200
Pathology of the Eye	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	IC	Lab Lec O AV	24	9/12/60 5/61	9/16/60	C 6 days	100
Recent Advances in Cataract Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	Lab PD LC Clin C Sem Surg Lec O AV TV EPP	1[illegible]	9/13/60	9/14/60	C 2 days	7[illegible]
Surgery of the Orbit	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 10	IC	Lab PD LC BR Surg Lec O AV IV EPP	7	9/16/60	9/16/60	C 1 day	3[illegible]

Key will be found on page 1670

OPHTHALMOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Glaucoma	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	PD Surg, Lec O AV, TV EPP	11	9/20/60	9/21/60	C 2 days	75
Perimetry	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary, New York 3	S	IC	PD Lec O AV, EPP	8	9/26/60 5/61	9/28/60	C 3 days	40
Keratectomies and Keratoplasties	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 30	IC	Lab PD Surg Lec O AV, TV, EPP	11	9/28/60	9/29/60	C 2 days	75
Enucleation and Evisceration	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	PD Surg, Lec O, AV, TV, EPP	7	9/30/60	9/30/60	C 1 day	35
Anomalies of Extraocular Muscles Including Ptosis	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary, New York 3	S Lim 10	IC	PD LC Surg Lec, O AV TV EPP	21	10/ 3/60	10/ 5/60	C 3 days	100
Clinical Problems of Tear Formation	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	PD, Lec O AV, EPP	2	10/ 6/60	10/ 6/60	C 1 day	10
Lacrimal Sac Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	IC	Lab PD Surg Lec, O AV, TV, EPP	7	10/ 6/60	10/ 6/60	C 1 day	35
Refraction	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 25	IC	PD Lec, O, AV, EPP	14	10/ 7/60	10/ 8/60	C 2 days	75
Biomicroscopy	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 8	IC	PD LC, Lec O AV EPP	15	10/17/60	10/21/60	C 5 days	75
Ocular Therapeutics	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	II	Lec O, AV	12	10/17/60	10/26/60	I 4 sessions 3 hr twice weekly Mondays Wednesdays	60
Uveitis	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	Lec, O AV	3	10/18/60	10/18/60	C 1 day	15
Gonioscopy and Tonography	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	IC	PD Lec O AV, EPP	3	10/18/60	10/18/60	C 1 day	15
Advances in Ocular Prostheses	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 10	II	PD, LC, Lec O, AV, EPP	4	10/19/60	10/26/60	I days unknown	20
Retinal Detachment	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	IC	PD Surg, Lec O, AV EPP	14	10/20/60	10/22/60	C, 3 days	75
Biomicroscopy Using Near Ultra Violet Cobalt Blue Polarized and Infra Red Lights	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	PD, LC, Lec, O AV, EPP	4	10/20/60	10/21/60	C 2 days	20
Radioisotopes in Ophthalmology	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	II	Lab PD Surg Lec O AV EPP	6	10/24/60	10/28/60	I 3 sessions 2 hr thrice Mondays Wednesdays Fridays	30
Complications of Ophthalmologic Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	II	Lab Lec O AV EPP	10	10/24/60	11/ 2/60	I 5 sessions 2 hr thrice weekly Mondays Wednesdays Fridays	50
Ocular Neuro Ophthalmology	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S	II	PD LC Lec O AV	10	10/25/60	11/ 8/60	I 5 sessions 2 hr twice weekly Tuesdays Thursdays	50

Ophthalmoscopy	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 8	II	PD LC Lec O AV EPP	16	10/25/60	11/17/60	I 16 sessions 2 hr twice weekly Tuesdays Thursdays	50
Light Coagulation (Meyer Schwickerath Apparatus)	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	Lab PD Surg Lec O AV EPP	4	10/27/60 1/61 or 2/61	10/28/60	C 2 days	0
Contact Lenses	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	IC	PD LC Lec O AV EPP	7	10/29/60 11/19/60	10/29/60	C 1 day	35
Entoptics and Macular Function Testing	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	II	PD Lec O AV EPP	4	10/31/60	11/ 2/60	I 2 sessions 2 hr twice weekly Mondays Wednesdays	20
Psychosomatic Factors in Ophthalmology	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	IC	Lec O AV	3	11/ 1/60	11/ 1/60	C 1 day	15
Physiological Optics	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	II	Lec O AV EPP	6	11/ 2/60	11/ 4/60	I 2 sessions 3 hr twice Wednesdays Friday	30
Ocular Geriatrics	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	IC	Lab Lec O AV	2	11/ 4/60	11/ 4/60	C 1 day	10
Ocular Photography	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 14	IC	Lab Lec O AV TV EPP	7	11/ 5/60	11/ 5/60	C 1 day	35
Ocular Radiology	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 9	IC	Lab PD LC Lec O AV EPP	6	11/ 7/60	11/10/60	C 4 days	30
Low Vision Aids	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 15	IC	PD Lec O EPP	4	11/10/60	11/11/60	C 2 days	20
Ocular Biochemistry	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 8	IC	Lab Lec O AV EPP	7½	11/14/60	11/18/60	C 5 days	35
Ocular Microbiology	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 8	IC	Lab Lec O AV EPP	6	11/14/60	11/17/60	C 4 days	30
Orthoptics	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 12	II	PD LC Lec O EPP	6	11/14/60	11/16/60	I 2 sessions 3 hr twice Monday Wednesday	30
Electrophysiology and Applied Physiology of the Eye	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 10	IC	Lab PD LC Lec O AV EPP	9	11/21/60	11/23/60	C 3 days	45
Clinical Bacteriology	Institute of Ophthalmology of the Americas 218 Second Ave New York course at New York Eye and Ear Infirmary New York 3	S Lim 8 for Lab	IC	Lab Lec O AV EPP	5	11/22/60	11/23/60	C 2 days	25
Ophthalmic Plastic Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 8	IC	Lab PD LC BR Clin C Surg Lec O AV EPP	100	4/61	5/61	C 15 days	250
Ocular Surgery	Institute of Ophthalmology of the Americas 218 Second Ave New York 3 course at New York Eye and Ear Infirmary New York 3	S Lim 20	IC	Lab PD LC Clin C Sem Surg Lec Pan O AV, TV EPP	52	5/61	One wk later	C 5 days	200
Ophthalmoscopy	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Jewish Chronic Disease Hospital Brooklyn N Y	G Lim 10	II	PD Lec	8	10/60	11/60	I 8 sessions 1 hr each days unknown	20
Ophthalmoscopy	New York University Post Graduate Medical School 0 First Ave New York	S	IC	PD Lec O AV	15	Arranged		C 5 days	60

Key will be found on page 1670

OPHTHALMOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
571 Theory and Practice of Contact Lenses	New York University Post Graduate Medical School 550 First Ave New York	S	IC	PD, Lec, O EPP	11	11/10/60	11/11/60	C 2 days	75
572 Surgery of the Cornea	New York University Post Graduate Medical School 550 First Ave New York	S Lim 10	IC	Lab PD LC Surg Lec, O AV, TV, EPP	35	11/14/60	11/18/60	C 5 days	250
573 Neuro Ophthalmology	New York University Post Graduate Medical School 550 First Ave New York	S	IC	PD Lec, O AV	15	1/23/61	1/27/61	C 5 days	55
574 Ophthalmic Plastic Surgery (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 15	IC	PD Surg Lec Pan O, AV, EPP	15	2/27/61	3/ 3/61	C 5 days	90
575 Motor Anomalies of the Eye (Part I) (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 25	IC	PD, Clin C Lec Pan O AV EPP	42	3/ 6/61	3/11/61	C 6 days	115
576 Motor Anomalies of the Eye (Part II) (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 16	IC	PD IC Clin C Lec, Pan O AV EPP	35	3/13/61	3/17/61	C 5 days	100
577 Surgery of the Eye (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York	S Lim 11	IC	Lab PD IC, Surg Lec Pan O, AV	42	3/20/61	3/25/61	C 6 days	140
579 Histopathology	New York University Post Graduate Medical School 550 First Ave New York	S	IC	Lab Lec O AV EPP	15	4/24/61	4/28/61	C 5 days	100
Ophthalmology	University of Cincinnati—College of Medicine Eden Avenue Cincinnati	G	IC	Sem Lec Pan O AV	4½	12/ 4/60	12/ 4/60	C 1 day	10
Newer Developments in Ophthalmology	Frank E Bunts Educational Institute 2020 E 93rd St, Cleveland 6	S Lim 125	IC	PD LC Clin C Lec Pan O, AV	12	12/ 7/60	12/ 8/60	C, 2 days	30
Ophthalmology Postgraduate Course	Ohio State University College of Medicine Columbus 10 Ohio	S	IC	Lec	14	3/ 6/61 Each March	3/ 7/61	C 2 days	20
Postgraduate Convention—Ophthalmology	Oregon Academy Ophthalmology and Otolaryngology and University of Oregon Medical School 1216 S W Yamhill St Portland 5 Ore course at University of Oregon Medical School Portland 1 Ore	S	IC	Lec Pan O AV	16	3/17/61	3/18/61	C 2 days	60 or 90 if combined with Otolaryngology course
Contact Lens Course	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas	S Lim 20	IC	Lab PD Sem Lec, O	28	5/22/61	5/25/61	C, 4 days	100
Thirty Fourth Annual Spring Congress in Ophthalmology and Otolaryngology	Gill Memorial Eye Ear and Throat Hospital 711 S Jefferson St Roanoke Va	S Lim 200	IC	Lab PD LC Clin C Sem Surg Lec O AV EPP	40	4/ 9/61	4/14/61	C 5½ days	80

ORTHOPEDIC SURGERY
(See also Anatomy)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Armed Forces Orthopedic Seminar	Walter Reed Army Institute of Research Walter Reed Army Medical Center Washington 12 D C	S Lim 200	IC	Sem Lec Pan O, AV	24	10/26/60	10/28/60	C, 3 days	Nil
Instructional Course Program—American Academy of Orthopaedic Surgeons	American Academy of Orthopaedic Surgeons 29 E Madison St Chicago course at Americana Hotel Bal Harbour Fla	S	IC	PD Clin C Sem Lec Pan, O AV	9	1/ 9/61	1/12/61	C 4 days	15
Orthopedic Basic Science	Northwestern University Medical School 303 E Chicago Ave, Chicago 11	S Lim 16	IC	Lab, PD IC BR Clin C Sem Lec	750	7/ 1/61	12/31/61	C 120 days	600
Orthopedics for the General Practitioner	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	IC	PD Lec O AV	7	2/22/61	2/22/61	C 1 day	10
What's New in Orthopedics	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City, Kan	B	IC	PD Lec Pan O AV	7	3/13/61	3/13/61	C 1 day	25
Orthopedic Surgery 2	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	S Lim 2	IC	Lab PD IC BR Clin C Sem Lec Pan O AV EPP	Variable	Arranged	Arranged	C Unknown	200 for 3 mo
Orthopedic Surgery 1	Harvard Medical School 25 Shattuck St Boston course at Children's Hospital Medical Center Boston	S Lim 5	IC	PD IC BR Clin C Sem O EPP	Variable	Arranged	Arranged	C Unknown	200 for 1 mo

Orthopedics for Specialists and General Physician	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	B	IC	Lec Pan O AV	15	12/ 1/60	12/ 3/60	C 3 days	40
Orthopedic Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Hospital for Crippled Children Unit of the United Hospitals of Newark Newark 4 N J	B Lim 40	II	Lec O AV	20	10/ 4/60	12/ 6/60	I 10 sessions 2 hr weekly Tuesdays	50
Minor Surgery and Office Orthopedics	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IO	PD LC Sem Lec Pan O AV EPP	14	12/14/60	12/15/60	C 2 days	30
Orthopedic Surgery PM 80—Pediatric Orthopedics	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Hospital for Joint Diseases New York 35	G	IO	PD Lec O AV	36	10/17/60	10/22/60	C 6 days	100
Orthopedic Surgery PM 1 Musculoskeletal Disease and Injury	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S	IC	Lec Pan O AV	35	11/14/60	11/18/60	C 5 days	100
Orthopedic Surgery PM 81 Foot Disabilities A Survey of the Diagnostic and Therapeutic Problems of the Foot	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Hospital for Joint Diseases New York 35	G	IC	PD Lec O AV	18	3/ 2/61	3/ 4/61	C 3 days	100
Orthopedics of the Foot	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S Lim 5	II	PD LC BR O Lec EPP	24	Arranged		I 8 sessions 1 day weekly	100
Basic Engineering for Orthopedic Surgeons	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec AV	10	9/26/60 1/ 2/61 5/12/61	10/26/60	I 10 sessions 1 hr twice weekly Mondays Wednesdays	100
Elementary Orthopedics Biomechanics	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec AV	15	9/26/60 1/ 2/61 5/12/61	10/26/60	I 15 sessions 1 hr twice weekly Mondays Wednesdays	150
Development of Posture and Postural Anomalies in Man	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	PD LC Clin C Sem Lec Pan O AV EPP	15	3/61	5/61	I 10 sessions 1½ hr twice weekly Tuesdays Thursdays	100
81 Orthopedics for the General Practitioner	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	II	PD BR Lec O AV EPP	16	10/ 4/60	11/29/60	I 8 sessions 2 hr weekly Tuesdays	45
82 The Surgical Rehabilitation of Arthritic Deformities	New York University Post Graduate Medical School 550 First Ave New York	S	IC	PD LC Lec AV EPP	21	11/16/60	11/18/60	C 3 days	75
91 Orthopedics in General Practice	New York University Post Graduate Medical School 550 First Ave New York	G Lim 20	IC	PD BR Lec O AV EPP	21	2/15/61	2/17/61	C 3 days	55
Orthopedics	University of Oregon Medical School 3181 S W Sam Jackson Park Rd Portland Ore	G Lim 15	IC	PD LC Clin C Surg Lec Pan O AV EPP	15	3/27/61	3/28/61	C 2 days	30

OTOLARYNGOLOGY

(See also Anatomy Endoscopy Pathology)

Symposium on Ear Nose and Throat Problems in Children	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco course at Children's Hospital San Francisco	G	IO	Lec Pan O AV	7	11/19/60	11/19/60	C 1 day	12 50
Clinical Otolaryngology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 4	PT	PD LC BR Clin C Surg O AV EPP	50	Arranged	2 wk later	10 days	60
Fellowship Demonstration Surgery	Northwestern University Medical School 303 E Chicago Ave Chicago 11	S Lim 2	PT	Lab PD LC BR Clin C Sem Surg Lec	960	Arranged		C 80 days	600
Basic Otologic Surgery Endaural Otologic Surgery — Audiology	Northwestern University Medical School 303 E Chicago Ave Chicago 11	S Lim 10	IO	Lab PD LC Clin C Sem Lec	200	2/ 6 61	3/11/61	C 5 wk	800
Annual Otolaryngologic Assembly—Current Trends in Otolaryngology	University of Illinois College of Medicine 1853 W Polk St Chicago 12 course at Illinois Eye and Ear Infirmary Chicago 7	S Lim 10	IC	Lab PD Clin C Sem Lec Pan O AV	64	9/24/60	9/30/60	C 7 days	125

Key will be found on page 1670

OTOLARYNGOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Bronchoesophagology	University of Illinois College of Medicine 1853 W Polk St, Chicago 12	S Lim 15	IC	Lab PD, LC, BR, Clin C, Sem Surg, Lec, O, AV, EPP	84	10/17/60 3/13/61	10/29/60	C 12 days	210
Anatomical and Clinical Otolaryngology	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	S	IC	Lab PD, Sem, Lec O AV, EPP	77	3/13/61	3/24/61	C 11 days	250
Clinical Traineeship in Otorhinolaryngology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S Lim 1	PT	Lab PD, BR Clin C Sem Lec, O, AV EPP	Unknown	Arranged	Unknown	Unknown —	50 mo Kansas residents 100 mo non residents
Otolaryngology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S	IC	Lec, Pan O, AV	17	4/10/61	4/12/61	C 3 days	40
Otolaryngology for General Practitioners	Tulane University School of Medicine 1430 Tulane Ave New Orleans	G Lim 50	IC	PD Lec Pan, O, AV	16	4/20/61	4/21/61	C 2 days	25
Otolaryngology	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	S Lim 60	IC	Lec, O, AV	18	4/20/61	4/22/61	C, 3 days	50
Home Study Course in Otolaryngology	American Academy of Ophthalmology and Otolaryngology 15 Second St S W, Rochester, Minn	S	HS(C)	Assigned reading	Self determined	9/ 1/60 9/ 1/61	6/30/61	Monthly assignments and exams by mail	20
Otolaryngology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study, Minneapolis	S	IC	Lec, Pan O AV	15	1/26/61	1/28/61	C 3 days	40
Otolaryngology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study, Minneapolis	G	IC	Lec Pan, O AV	15	4/20/61	4/22/61	C, 3 days	40
Allergy and Immunity in Otolaryngology	Hansel Foundation 634 N Grand Blvd, St Louis course at Park Plaza Hotel, St Louis	G Lim 50	IC	Lab Lec, Pan O	35	5/30/61	6/ 3/61	C, 5 days	150
Otolaryngology	University of Buffalo School of Medicine 3435 Main St Buffalo 14 N Y	G	IC	PD Sem Lec Pan O AV EPP	14	9/28/60	9/29/60	C 2 days	30
Otorhinolaryngology PM 30—Trans meatal (endaural) Surgery	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 9	IC	Lab Surg Lec O, AV EPP	80	9/ 6/60 3/27/61	9/17/60	C 10 days	350
Otorhinolaryngology PM 33—Rhinoplasty and Otoplasty	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	IC	Lab IC Surg Lec, O AV	112	1/ 7/61	1/21/61	C 14 days	350
Otorhinolaryngology PM 32—Combined Course in (a) Indirect Laryngoscopy and Voice Rehabilitation and (b) Audiology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	IC	PD IC Sem Surg	21 per section	2/ 6/61 Section B 2/ 9/61	2/ 8/61	C 6 days (both sections)	75 per section 150 for entire course
Otorhinolaryngology PM 34—Head and Neck (including laryngeal) Surgery	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 6	IC	Lab PD Sem Surg	77	2/13/61	2/24/61	C 11 days	350
Otolaryngology PM 2—Histopathology of the Ear Nose and Throat	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S	II	Lab Lec AV EPP	12	4/11/61	4/27/61	I 6 sessions 2 hr weekly Tuesdays Thursdays	100
Otorhinolaryngology PM 31—Stapes Surgery	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 6	IC	Lab PD Clin C Surg EPP	105	4/17/61	5/ 5/61	C 15 days	[illegible]00
[illegible] Advance[illegible] Course in Functional [illegible] Surgery [illegible]	New York University Post-Graduate Medical School [illegible] First Av [illegible] New York	S Lim [illegible]	IC	Lab Lec O EPP	70	11/ 9/60	11/18/60	C 10 days	[illegible]00

7 Laryngology and Surgery of the Larynx and Neck	New York University Post Graduate Medical School 550 First Ave New York	S Lim 10	IC	Lab PD LC Sem Surg Lec Pan O AV EPP	70	1/ 9/61	1/20/61	C 10 days	250
78 Endaural Surgery	New York University Post Graduate Medical School 550 First Ave New York	S Lim 8	IC	Lab PD Sem Lec Pan O AV EPP	70	2/13/61	2/21/61	C 10 days	27[illegible]
[illegible] Audiology	New York University Post Graduate Medical School 550 First Ave New York	S Lim 15	IC	PD LC Clin C Sem Lec Pan O AV EPP	21	2/27/61	3/ 1/61	C 3 days	[illegible]0
[illegible] Neuro Otology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 10	IC	PD LC Clin C Sem Lec Pan O AV EPP	21	3/ 2/61	3/ 4/61	C 3 days	50
Twenty Fifth Annual Graduate Convention in Otology Rhinology and Laryngology—Regional Anatomy and Cadaver Surgery in the Field of Otolaryngology	University of Cincinnati College of Medicine Eden and Bethesda Avenues Cincinnati 19	S Lim 24	IC	Lab PD LC Clin C Sem Surg Lec O AV EPP	45	4/10/61 Annually	4/14/61	C 5 days	1[illegible]0
Postgraduate Convention—Otolaryngology	Oregon Academy Ophthalmology and Otolaryngology and University of Oregon Medical School 1216 S W Yamhill St Portland 5 Ore course at University of Oregon Medical School Portland 1 Ore	S	IC	Lec Pan O AV	16	3/16/61	3/17/61	C 2 days	60 or 90 if combined with Ophthalmology course
Otosclerosis Surgery and Tympanoplasty	Temple University Philadelphia 40	S Lim 4	IC	Lab PD LC Clin C Sem Surg Lec Pan O AV EPP	140 or more	Arranged	Arranged	C 14 days or more	800
Laryngology and Laryngeal Surgery	Temple University School of Medicine and Hospital 3400 N Broad St Philadelphia 40	B Lim 12	IC	Lab PD LC Clin C Sem Surg Lec Pan O EPP	80	9/26/60 4/10/61	10/ 7/60	C 11 days	250
Audiometry for Office and Industry	Temple University School of Medicine 3400 N Broad St Philadelphia 40	S Lim 25	IC	PD Lec O AV EPP	32	6/61	Unknown	C 5 days	100

PATHOLOGY

(See also Malignant Disease Obstetrics and Gynecology Radiology Urology)

Neuropathology	University Extension—University of California Los Angeles University of California Medical Center Los Angeles 24	B	II	Lab Lec AV EPP	28	10/18/60	12/ 6/60	I 14 sessions 2 hr each Tuesday and Thursday	10[illegible]
Advances in Ophthalmic and General Pathology	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus San Francisco	S	IC		18	11/ 3/60	11/ 5/60	C 3 days	Unknown
Hepatic Pathology	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	S Lim 20	IC	Lab Lec AV	40	8/61	8/61	C Unknown	100
Pathology 60—Brain Tumor Registry	Yale University School of Medicine 333 Cedar St New Haven Conn	S in Neurosurg neurology neuropath	IC	Sem O AV	Arranged	Arranged	Unknown	C Arranged	Arranged
Workshop in Resident Training in Pathology	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	S Military Only Lim 20	IC	Sem O AV	21	9/12/60	9/14/60	C 3 days	Nil
Orthopedic Pathology	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	S Military personnel Only Lim 25	IC	Lab Clin C Lec O AV EPP	210	10/31/60	12/ 9/60	C 40 days	Nil
Forensic Sciences Symposium	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	G Lim 120	IC	Lec Pan O AV TV EPP	21	11/ 8/60 5/ 2/61	11/10/60	C 3 days	Nil
Forensic Pathology	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	S Lim 75	IC	Lab Sem Lec Pan O AV TV EPP	35	1/23/61	1/27/61	C 5 days	Nil
Annual Armed Forces Institute of Pathology Lectures 1961	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	B Lim 120	IC	Lec O AV TV EPP	30	2/13/61	2/17/61	C 5 days	Nil
Ophthalmic Pathology	Armed Forces Institute of Pathology 6825 16th St N W Washington 12 D C	S Lim 55	IC	Lab Lec O AV TV EPP	35	3/13/61	3/17/61	C 5 days	Nil
Cancer Cytology Training for Physicians and Cytologists	Cancer Cytology Foundation of America Inc 1700 Biscayne Blvd Miami Fla	S and non M D	IC	Lab PD Clin C, Sem Lec AV	960	1/ 1/61 6/ 1/61	6/ 1/61	C 5 days wk for 6 mo	350
Surgical Pathology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 9	IC	Lab Clin C Sem Lec O AV EPP	48	Arranged	2 wk later	C 12 days	150
Surgical Pathology for Specialty Board Candidates	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim [illegible]	IC	Lab Clin C Sem Lec O AV EPP	38 hr per wk	Arranged	2 or 4 wk later	C 6 12 18 or 24 days	150 to 250
Surgical Pathology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 9	PT	Lab Clin C Sem Lec O AV EPP	96	Arranged	4 wk later	24 days	250

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PATHOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship in Pathology	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City, Kan	B Lim 1	PT	Lab PD BR, Clin C Sem, Lec O, AV, EPP	Unknown	Arranged	Unknown	Unknown	50 mo Kansas residents 100 mo non residents
Neuropathology	Postgraduate Committee University of Maryland School of Medicine 522 W Lombard St, Baltimore	S Path Lim 2	IC	Lab, Clin C, Lec O		Arranged		C 6 months	200 plus 10 lab fee
Neuropathology and Techniques	University of Maryland School of Medicine—Postgraduate Section 522 W Lombard St Baltimore	S Path Lim 18	II	Lab Clin C Sem O	40	12/60	5/61	I 4 10 hr sessions 4 week ends of late Friday through Saturday	125
Pathology with Clinical Application	The University of Michigan Medical School Department of Postgraduate Medicine 1610 University Hospital Ann Arbor, Mich	S Lim 10	IC	Lab PD Clin C Lec, O AV	340	9/26/60	12/16/60	C, 60 days	250
Urologic Pathology	Wayne State University College of Medicine 1401 Rivard St Detroit	S Lim 25	II	Lab, Sem, Lec AV	64	9/60	2/61	I 16 sessions 4 hr weekly Mondays	90
Gynecologic Pathology	Wayne State University College of Medicine 1401 Rivard St, Detroit	S Lim 25	II	Lab Sem Lec, AV	64	9/60	2/61	I 16 sessions 4 hr weekly Wednesdays	90
Seminar in Surgical Pathology	Wayne State University College of Medicine 1401 Rivard St Detroit	S Lim 25	II	Lab Sem Lec, AV	32	9/60 1st day of 2nd semester	2/61	I 16 sessions 2 hr weekly Thursdays	45
Dermatopathology Seminar	Department of Dermatology Wayne State University College of Medicine 1401 Rivard St Detroit	S derm path	II	Lab Sem Lec O EPP	40	9/12/60	6/14/61	I 40 sessions schedule unknown	45
Dermatopathology	Wayne State University College of Medicine 1401 Rivard St, Detroit	S derm path	II	Lab Clin C, Sem Lec AV	64	2/61	6/61	I 16 sessions 4 hr weekly Fridays	90
Neuropathology	Wayne State University College of Medicine 1401 Rivard St Detroit	S Lim 25	II	Lab, Sem Lec AV	64	2/61	6/61	I 16 sessions 4 hr weekly Mondays	90
Pathology of Neoplasms	Wayne State University College of Medicine 1401 Rivard St, Detroit	S Lim 25	II	Lab, Sem Lec, AV	64	2/61	6/61	I 16 sessions 4 hr weekly Wednesdays	90
Histopathology of Ear Nose and Throat	Wayne State University College of Medicine 1401 Rivard St, Detroit	S Lim 25	II	Lab, Sem Lec AV	32	2/61	6/61	I 16 sessions 2 hr weekly Fridays	45
Directed Study in Clinical Pathology and Pathologic Anatomy	Wayne State University College of Medicine 1401 Rivard St, Detroit	S	IC	Lab Clin C Sem, AV, EPP	2000	7/ 1/61	6/30/62	C 300 days	90
Clinical Gynecology and Gynecologic Pathology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at St Michael's Hospital Newark N J	G Lim 45	II	Lec O, AV	12	9/28/60	11/ 7/60	I 6 sessions 2 hr weekly Wednesdays	35
Forensic Medicine	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	Sem Lec, Pan, O, AV, EPP	7	12/ 8/60	12/ 8/60	C 1 day	15
Applied Gynecologic Pathology	Long Island Jewish Hospital 270 05 76th Ave New Hyde Park, New York	S Lim 10	II	Lab, Clin C, Lec	42	10/ 6/60 10/61	1/ 5/61	I 14 sessions 3 hr weekly Thursdays	100
Pathology GM 1—Surgical Pathology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	G	IC	Lab PD, Clin C, EPP		Arranged First day each mo	6 or 12 mo later	C 6 or 12 mo	300 for 6 mo 600 for 12 mo
Pathology PM 31—Surgical Pathology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	II	Lab Lec O, AV	30	9/10/60	12/17/60	I 15 sessions 2 hr weekly Saturdays	100
Pathology PM 30—General and Special Pathology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	II	Lab Lec O	30	9/17/60	12/24/60	I 15 sessions 2 hr weekly Saturdays	100
Surgical Pathology—Gyn [illegible] and Surgical	New York Medical College Flower and Fifth Avenue Hospitals [illegible] 106th St New York	S Lim 9	II	Lab Lec O AV	90	Arranged	Unknown	I 30 sessions 3 hr each	200

Obstetrical and Gynecological Pathology	New York Polyclinic Hospital 345 W 50th St New York 19	S Lim 10	IC	Lab PD LC BR Clin C Lec O EPP	30	Arranged	Unknown	C 10 days	50
Urological Pathology	New York Polyclinic Hospital 345 W 50th St New York 19	S Lim 10	IC	Lab PD LC Clin C Lec EPP	30	Arranged	Unknown	C 10 days	50
Surgical Pathology	New York Polyclinic Hospital 345 W 50th St New York 19	C Lim 10	IC	Lab PD LC BR Clin C Lec EPP	50	10/ 1/60 4/ 1/60	10/30/60	C 21 days	50
Dermal Pathology	Skin and Cancer Hospital of Philadelphia 801 Pine St Philadelphia	S	IC	Lec Pan O AV	40	2/13/61	2/17/61	C 5 days	100
General Oncology	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G	II	Lec	30	9/ 3/60	4/ 1/61	I 30 sessions 1 hr weekly Saturdays	Nil
Forensic Pathology	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G	II	Lec	20	9/22/60	6/22/61	I 20 sessions 1 hr alternate Thursdays	Nil
Pathology and Pathogenesis of Human Tumors	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at M D Anderson Hospital and Tumor Institute Houston 25 Texas	G and residents Lim 25	II	Lec EPP	25	10/ 5/60	3/22/61	I 25 sessions 1 hr weekly Wednesdays	30

PEDIATRICS

(See also Allergy Chest Diseases Dermatology Ephebology Hematology Malignant Disease Neurology Orthopedic Surgery Otolaryngology Psychiatry)

Emotional Problems in Pediatric Practice	University Extension—University of California Los Angeles University of California Medical Center Los Angeles course at University of California Conference Center Lake Arrowhead Calif	B	IC	Sem Lec Pan O AV	13	7/61	Unknown	C 3 days	Unknown
General Pediatrics—Infectious Diseases Neurology	American Academy of Pediatrics 1801 Hinman Ave Evanston Ill course at University of California Medical Center San Francisco 2	S	IC	Lec Pan O AV	20	3/61	Unknown	C 3 days	40 members 60 non members
Perinatal Problems	Continuing Education in Medicine and the Health Sciences University of California Medical Center Second and Parnassus San Francisco course at Children's Hospital San Francisco	G	IC	Lec Pan O AV	7	3/11/61	3/11/61	C 1 day	12 50
Management of Acute Pediatric Problems	American Academy of Pediatrics 1801 Hinman Ave Evanston Illinois course at Hospital for Sick Children Toronto Canada	S	IC	Lec Pan O	20	5/29/61	5/31/61	C 3 days	40 members 60 non members
In Residence Post Graduate Course for General Practitioners	The Children's Hospital 1056 E 19th Ave Denver 18	G	PF	PD IC BR Clin C Lec O AV	44	11/14/60 3/13/61 8/14/61 11/13/61	11/19/60	5½ days	25
Clinical and Research Advances in Pediatrics and Child Guidance	Office of Postgraduate Medical Education University of Colorado Medical Center 1200 E Ninth Ave Denver 20 course at The Stanley Hotel Estes Park Colo	S Lim 300	IC	Sem Lec Pan O AV	36	9/ 1/60	9/ 6/60	C 6 days	60 full course 30 either part plus 10 regis
Pediatric Postgraduate Day	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	B	II	PD IC Clin C Sem Lec Pan O AV	36	10/ 7/60	5/ 5/61	I 9 sessions 1st Friday each mo	Nil
Clinical and Research Advances in Pediatrics and Child Guidance	Office of Postgraduate Medical Education University of Colorado Medical Center 1200 E Ninth Ave Denver 20 course at The Stanley Hotel Estes Park Colo	S Lim 300	IC	Sem Lec Pan O AV	36	8/24/61	8/29/61	C 6 days	60 full course or 30 either part plus 10 regis
Emotional Problems in Children	American Academy of Pediatrics 1801 Hinman Ave Evanston Ill course at Yale University Child Study Center New Haven 11 Conn	S	IC	Lec Pan O AV	20	11/28/60	11/30/60	C 3 days	40 members 60 non members
Postgraduate Course in Pediatric Allergy	Children's Hospital of D C 2125 13th St N W Washington 9 D C	S Lim 180	IC	PD IC Lec O AV EPP	12	4/ 8/61	4/ 9/61	C 2 days	50
Pediatric Allergy	American Academy of Pediatrics 1801 Hinman Ave Evanston Ill course at Children's Hospital of District of Columbia Washington 9 D C	S	IC	Unknown	Unknown	Unknown	Unknown	C Unknown	40 members 60 non members

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PEDIATRICS—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Seminar in Pediatrics	University of Florida College of Medicine Gainesville Florida	B	IC	LC Clin C, Sem Lec Pan O	15	2/61	Unknown	C 2½ days	25
Problems of the Newborn Infant	Medical College of Georgia Augusta, Ga	G	IC	PD LC Clin C, Sem Lec Pan	18	1/24/61	1/26/61	C 2 days	50
Clinical Pediatrics	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 4	PI	PD LC BR Clin C O AV FPP	120	Arranged	4 wk later	20 days	125
Course V—Pediatrics	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 25	IC	PD LC BR Clin C Lec O AV FPP	70	10/ 3/60 4/10/61	10/14/60	C 11 days	150
Pediatrics	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	G	IC	Lec O AV	7	12/ 7/60	12/ 7/60	C 1 day	10
Pediatrics	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IC	PD Lec, Pan O AV	10	9/14/60	9/15/60	C 1½ days	20
Clinical Traineeship in Pediatrics	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City Kan	B Lim 2	PT	Lab PD LC, BR Clin C Sem Lec O AV FPP	Unknown	Arranged	Unknown	Unknown	50 mo Kansas residents 100 mo non-residents
Pediatrics	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City Kan	B	IC	PD LC Clin C Lec Pan, O AV	21	3/ 6/61	3/ 8/61	C 3 days	45
Annual Pediatric Postgraduate Course	Department of Pediatrics University of Louisville Medical School 323 E Chestnut St Louisville 2 Ky course at Children s Hospital, Louisville 2 Ky	G Lim 30	II	Lab PD LC Clin C Sem Lec Pan O AV	24	4/11/61	5/30/61	I 8 sessions 3 hr weekly	30
Pediatric Postgraduate Course	University of Louisville School of Medicine Department of Pediatrics 323 E Chestnut Louisville 2 Ky course at Children s Hospital, Louisville 2 Ky	G	II	PD BR Sem, Lec Pan O	24	4/11/61	5/30/61	I 8 sessions 3 hr alternate Tuesdays	30 or 5 per day
Newer Concepts of Cardiorespiratory Disease in Children	Tulane University School of Medicine 1430 Tulane Ave New Orleans	G Lim 25	IC	PD BR Clin C Lec O AV, EPP	20	4/13/61	4/15/61	C 2½ days	35
Pediatrics 1	Harvard Medical School 25 Shattuck St, Boston course at Massachusetts General Hospital Boston	B Lim 3	IC	PD LC, BR Clin C Sem Lec O FPP	122, 1400	10/ 3/60	5/31/61	C Unknown	100 a mo
Pediatrics 2	Harvard Medical School 25 Shattuck St Boston course at Children s Hospital Medical Center Boston	B Lim 10	IC	Lab, PD LC, BR Clin C Sem Lec Pan O AV, FPP	1540	10/ 3/60	3/31/61	C, 155 days	750
Pediatrics 4	Harvard Medical School 25 Shattuck St Boston course at Children s Hospital Medical Center Boston	B Lim 75	IC	PD LC BR, Clin C Sem, Lec Pan O AV EPP	40	1/23/61	1/27/61	C 5 days	125
Pediatrics 3	Harvard Medical School 25 Shattuck St, Boston course at Massachusetts General Hospital Boston	B Lim 150	IC	PD LC Clin C Sem Lec O	70	6/ 5/61	6/16/61	C 11 days	200
Pediatric Metabolism and Endocrinology	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital, Boston	B Lim 150	IC	PD LC, Clin C Sem Lec O	28	6/13/61	6/16/61	C 4 days	100
Pediatrics	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	G Lim 40	IC	PD Clin C Lec, O AV	18	1/23/61	1/25/61	C 3 days	30
Pediatrics for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	S	IC	Lec, Pan, O, AV	18	9/ 6/60	9/ 8/60	C 3 days	40
Pediatrics for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec, Pan O AV	15	2/27/61	3/ 1/61	C 3 days	40
Allergy and Immunity in Pediatrics	Hansel Foundation 634 N Grand Blvd St Louis course at Park Plaza Hotel St Louis	S Lim 60	IC	Lab Lec Pan O	35	5/30/61	6/ 3/61	C 5 days	150
General Pediatrics	American Academy of Pediatrics 1801 Hinman Ave Evanston Ill course at Washington University St Louis	S Lim 75	IC	Lec Pan O AV	20	6/ 6/61	6/ 8/61	C 3 days	10 members 60 non-members

Pediatric Allergy & Hematology	University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IO	LC BR Clin C Sem Lec Pan O AV	12	4/17/61	4/19/61	C 3 days	30
Recent Advances in Pediatrics	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St, Newark 2, N J course at Babies Hospital Unit of The United Hospitals of Newark Newark, N J	G Lim 6	II	PD Clin C Lec O AV	16	10/ 7/60	12/16/60	I 11 sessions 1½ hr weekly Fridays	50
Pediatrics	University of Buffalo School of Medicine 3435 Main St, Buffalo	G	II	PD Sem Lec Pan O AV EPP	15	10/ 5/60	11/ 9/60	I 6 sessions 2½ hr weekly Wednesdays P M	60
Pediatrics	Joint Committee on Post Graduate Education 1313 Bedford Ave, Brooklyn, N Y course at Coney Island Hospital Brooklyn, N Y	C Lim 25	II	LC Lec	15	10/60	12/60	I 10 sessions 1½ hr each days unknown	30
Kidney Disease in Childhood	Maimonides Hospital of Brooklyn 4802 Tenth Ave, Brooklyn 19, N Y	C Lim 6	II	PD LC BR Clin C Sem Lec AV	24	1/ 3/61 4/ 5/61	3/ 3/61	I 16 sessions 1½ hr twice weekly Tuesdays Thursdays	50
Postgraduate Pediatric Oncology	Memorial Cancer Center 444 E 68th St, New York	S Lim 20	II	PD LC BR Sem Lec	16	10/ 7/60 11/18/60	11/25/60	I 8 sessions 2 hr weekly Fridays	Nil
Three Day Course in Pediatric Oncology	Memorial Cancer Center 444 E 68th St, New York	S Lim 20	IC	PD LC BR Clin C Sem Lec Pan	21	4/26/61 Spring 1962	4/28/61	C 3 days	35
611 Seminar on General Pediatrics	New York University Post Graduate Medical School 550 First Ave, New York	G	II	LC Clin C Sem Lec Pan AV	36	9/28/60	5/24/61	I 18 sessions 2 hr weekly Wednesdays	125
Advances in Pediatrics	Rochester Regional Hospital Council 150 East Ave, Rochester 7, N Y course at University of Rochester Medical Center, Rochester 20, N Y	B Lim 20	IC	PD BR Sem Pan O AV	15	10/12/60	10/14/60	C 3 days	45
Pediatric Endocrinology	American Academy of Pediatrics 1801 Hinman Ave, Evanston, Ill course at State University of New York Upstate Medical Center, Syracuse 10, N Y	S	IC	PD Lec Pan O	20	11/ 9/60	11/11/60	C 3 days	40 members 60 non members
Pediatrics	University of Oregon Medical School 3181 S W Jackson Park Rd Portland, Ore	G	IC	PD LC Clin C Lec Pan O AV	15	2/20/61	2/21/61	C 2 days	30
Tenth Annual Postgraduate Seminar for Pediatricians	St Christopher's Hospital for Children 2600 N Lawrence St, Philadelphia, Pa	S	IC	PD LC BR Clin C Sem Lec Pan O AV TV	25 30	5/24/61	5/27/61	C 4 days	75
Tenth Annual Postgraduate Seminar for Pediatricians	St Christopher's Hospital for Children 2600 N Lawrence St, Philadelphia, Pa	S	IC	PD LC BR Clin C Sem Lec Pan O AV TV	25 30	5/24/61 Annually	5/27/61	C 4 days	75
Pediatrics for the General Practitioner	Postgraduate Department, University of Tennessee College of Medicine 62 S Dunlap St, Memphis, Tenn	G Lim 4	IC	PD LC BR Clin C Sem Lec Pan O AV EPP	10	3/ 6/61	3/10/61	C 5 days	65
Pediatric Cardiology	American Academy of Pediatrics 1801 Hinman Ave, Evanston, Ill course at Texas Children's Hospital Baylor University, Houston, Texas	S	IC	Lec Pan O AV	20	2/16/61	2/18/61	C 3 days	40 members 60 non members
Postgraduate Refresher Course in Pediatrics	Scott and White Memorial Hospital and Scott, Sherwood and Brindley Foundation Temple Division, University of Texas Postgraduate School of Medicine 13 W Avenue C, Temple, Texas	G Lim 1	PT	PD LC BR EPP	176	First Monday of mo September through August annually	Last Saturday of mo	24 days	25
Pediatrics	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center, Houston, Texas course at Scott and White Clinic Temple, Texas	G Lim 2	PT	PD LC BR Sem Surg O EPP	176	9/12/60 First Monday of each mo	10/ 1/60	24 days	25
Seminars on Child Behavior Problems and Teenage Problems	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center, Houston 25, Texas course at San Antonio, Texas	B Lim 20	CO	Unknown	12			I 2 sessions 6 hr each Saturdays Sundays	Unknown
	El Paso, Texas San Angelo, Texas Austin, Texas Temple, Texas Beaumont, Texas Lubbock, Texas Texarkana, Texas Corpus Christi, Texas Houston, Texas					9/17/60 10/ 8/60 11/ 5/60 1/14/61 2/ 4/61 3/ 4/61 5/27/61 6/24/61 7/ 8/61 8/26/61	9/18/60		

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PEDIATRICS—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pediatric Allergy	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at Turner Home El Paso Texas	B Lim 60	IC	Lec Pan O AV	7	5/20/61	5/20/61	C 1 day	10
Growth Failure in Children	University of Washington School of Medicine Seattle	S Lim 30	IC	Lab PD LC BR Sem Lec Pan O AV FPP	Unknown	9/ 8/60	9/10/60	C 2½ days	45

PERIPHERAL VASCULAR DISEASES
(See also Surgery)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Management of Your Patient with Vascular Disease	Medical College of Georgia Augusta Ga	G Lim 20	IC	PD LC Clin C Sem Lec Pan	18	2/28/61	3/ 2/61	C 3 days	50
Treatment of Varicose Veins	Cook County Graduate School of Medicine 707 S Wood St Chicago	G Lim 12	IC	Lab PD LC BR Surg Lec AV TV FPP	18	9/26/60 10/24/60 1/30/61 3/20/61 7/17/61	9/30/60	C 5 days	100
Femoral Arteriography and Aortography	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 4	IC	Lab PD LC Surg Lec AV FPP	12	10/ 4/60 11/15/60 six starting dates in 1961 to be announced	10/ 7/60	C 4 days	100
Medicine PM 65	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32 course at Montefiore Hospital New York 67	G Lim 15	II	PD LC BR, Lec Pan O AV, EPP	63	9/20/60	1/31/61	I 21 sessions 3 hr weekly Tuesdays	100
Peripheral Vascular Diseases	Joint Committee on Post Graduate Education 1313 Bedford Ave, Brooklyn, N Y course at Coney Island Hospital Brooklyn, N Y	G Lim 25	II	LC Lec	10	10/60	12/60	I 10 sessions 1 hr each days unknown	20
Peripheral Vascular Diseases	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn, N Y course at Jewish Hospital Brooklyn N Y	G Lim 20	II	PD Lec	10	4/61	5/61	I 10 sessions 1 hr each, days unknown	20
Principles and Treatment of Peripheral Vascular Diseases	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital New York 29	G Lim 15	II	PD Sem Lec	18	9/60 3/61	1/61	I 12 sessions 1½ hr alternate Mondays	150
Peripheral Vascular Diseases	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	S Lim 50	IC	Sem Lec Pan, O AV	24	6/22/61	6/24/61	C 3 days	75

PHYSICAL MEDICINE AND REHABILITATION

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Physical Medicine and Rehabilitation in General Practice	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	B	IC	PD, LC, Lec Pan O AV	24	6/61	6/61	C 3 days	35
Physical Therapy and Occupational Therapy in the Care of Neuro Muscular Disease	Georgia Warm Springs Foundation Warm Springs Ga	G Lim 18	IC	PD LC, Lec Pan O, AV FPP	480	9/26/60 3/27/61	12/16/60	C 90 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro Muscular Disease	Georgia Warm Springs Foundation Warm Springs Ga	G Lim 18	IC	PD LC Lec, Pan, O AV FPP	960	9/26/60 3/27/61	3/24/61	C 180 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro Muscular Disease	Georgia Warm Springs Foundation Warm Springs Ga	G Lim 35	IC	PD LC Lec Pan O FPP	36	9/26/60 3/27/61	9/30/60	C 5 days	Nil
Clinical Traineeship in Physical Medicine	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 1	PT	Lab PD LC BR Clin C Sem Lec O AV, EPP	Unknown	Arranged	Arranged	Unknown	50 mo Kansas residents 100 mo non residents
Physical Medicine for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14	S	IC	PD Lec Pan O AV	15	11/ 7/60	11/ 9/60	C 3 days	40
Physical Medicine	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IC	PD LC BR Clin C Sem Lec Pan O AV	6	10/ 7/60	10/ 7/60	C 1 day	15
Physical Medicine and Rehabilitation GM 1	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York	G Lim 3	IC	PD Clin C AV		Arranged first day each mo	6 or 12 mo later	C Unknown	300 for 6 mo 600 for 12 mo

Kinesiology 30	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	G Lim 30	II	Lec O AV	32	[illegible]/11/61	[illegible]	I 16 sessions [illegible] hr weekly Saturdays	80
Geriatric Rehabilitation—Rehabilitation of Chronically Ill Patients	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Bird S Coler Hospital New York 17	G Lim 100	IC	PD LC BR Clin C Sem Lec O FPP	Unknown	11/14/60	11/18/60	C 5 days	100
C 1 Physical Medicine and Rehabilitation	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 30	IC	LD Lec	70	10/10/60	10/21/60	C 10 days	110
Six Month Postgraduate Course in Physical Medicine and Rehabilitation	Highland View Hospital 3901 Ireland Drive Cleveland 22	G	PT	PD LC BR Clin C Sem Lec AV EPP	400	7/ 1/61 7/62	12/31/61	178 days	Nil
PROCTOLOGY									
Proctology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G Lim 30	IC	Lec Pan O AV FPP	30	5/15/61	5/19/61	C 5 days	65
Proctology PM 30	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G	IC	Lec O AV	10	11/ 3/60 4/13/61	11/ 4/60	C 2 days	25
Coloproctology (Operative Demonstrations and Cadaver)	New York Polyclinic Hospital 345 W 50th St New York 19	S surg Lim 10	IC	Lab PD LC BR Lec O EPP	25	10/ 1/60 4/ 1/61	10/ 5/60	C 5 days	60
Proctology	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at Scott and White Clinic Temple Texas	G Lim 2	PI	PD LC BR Sem Surg O FPP	88	Arranged	Unknown	12 days	25
PSYCHIATRY									
Psychiatry in Medicine	University Extension -University of California Los Angeles University of California Medical Center Los Angeles	B	IC	LC Sem Lec AV	13	3/10/61	3/11/61	C 2 days	Nil
Brief Psychotherapy Seminars	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant Street Palo Alto Calif	S Lim 10	II	Sem Lec	20	Unknown	Unknown	I schedule unknown	Unknown
Family Therapy Seminars	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant St Palo Alto Calif	S Lim 12	II	LC Sem FPP	12	10/10/60	12/19/60	I 6 sessions 2 hr Mondays	Unknown
Psychiatry in General Practice	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant St Palo Alto Calif	B Lim 20	II	Sem Lec	16	11/16/60	3/ 1/61	I 8 sessions 2 hr Wednesdays	Unknown
Function of Mind in Light of Present Day Ego	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant St Palo Alto Calif	S Lim 10	II	Sem Lec	20	1/10/61	5/ 2/61	I 10 sessions 2 hr Tuesdays	Unknown
Behavioral Science Survey Lectures	Mental Research Institute Palo Alto Medical Research Foundation 860 Bryant St Palo Alto Calif	S Lim 20	II	Sem Lec	18	1/19/61	4/27/61	I 9 sessions 2 hr Thursdays	Unknown
Recognition and Management of Responses to Critical Events—Psychiatric Implication in Medical Practice	Langley Porter Neuropsychiatric Institute 401 Parnassus Ave San Francisco course at University of California Medical Center San Francisco	G Lim 100	IC	Lec Pan O AV	12	1961	2 days later	C 3 days	Unknown
Psychiatry in Medical Practice	The Langley Porter Neuropsychiatric Institute 401 Parnassus Ave San Francisco	G Lim 12	II	PD Clin C Sem O FPP	60	2/61 4/61	12 wk later	I 12 sessions 5 hr weekly Wednesdays	25
Psychoanalytic Theory and Practice	San Francisco Psychoanalytic Institute 2180 Sutter St San Francisco 15	S	II	Sem Lec O	Unknown	Unknown	Unknown	I 2 3 hr sessions a mo	Unknown
Clinical Interpretation of Rorschach Test	Department of Psychology University of Chicago 5730 Ellis Ave Chicago 37	B	PF	PD Sem Lec	30 per wk	7/10/61	7/21/61	10 days	Unknown
Psychopathology for the General Practitioner	North Shore Hospital 225 Sheridan Rd Winnetka Ill	G	II	Sem Lec O	Unknown	10/60	6/61	I 9 sessions 2 hr biweekly Wednesdays	Nil
Psychiatry for General Practitioners	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	G	II	PD LC Lec O	12	10/ 5/60 4/ 5/61 5/17/61	10/26/60	I 4 sessions 3 hr weekly Wednesdays	30

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PSYCHIATRY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeship in Psychiatry	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City, Kan	B Lim 2	PT	PD BR Clin C Sem, Lec O AV EPP	Unknown	Arranged	Unknown	Unknown	Unknown
Psychiatry (Medical Surgical Clinical Symposia)	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	Lec Pan O AV	7	3/24/61	3/24/61	C 1 day	20
Psychiatry for Internists	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	B Lim 12	II	PD Sem Lec O AV	24	10/12/60	1/11/61	I 12 sessions 2 hr weekly Wednesdays	60
Psychiatry	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital Ann Arbor Mich	G Lim 10	IC	PD Clin C Lec O AV	12	2/20/61	2/21/61	C 2 days	30
Introductory Psychiatry	Lafayette Clinic 951 E Lafayette Detroit	G	PT	PD Clin C Lec O	60	9/20/60	5/23/61	30 days	Nil
Child Psychiatry for General Practitioners and Pediatricians	Wayne State University College of Medicine 1401 Rivard Detroit 7	G Lim 15	II	LC Clin C Sem Lec	27	9/29/60 2/ 9/61	2/ 2/61	I 18 sessions 1½ hr weekly Thursdays	33 75
Medical Psychiatric Seminar	Wayne State University College of Medicine 1401 Rivard Detroit 7 course at Detroit Receiving Hospital, Detroit 26	G Lim 10	II	PD LC Clin C O	9	9/30/60 2/10/61	2/ 3/61	I 6 sessions 1½ hr monthly Fridays	33 75
Pediatric Psychiatric Seminar	Wayne State University College of Medicine 1401 Rivard Detroit 7 Detroit Receiving Hospital Detroit 26	G Lim 10	II	PD LC Clin C O	6	10/ 7/60 2/17/61	1/13/61	I 4 sessions 1½ hr monthly Fridays	33 75
Surgical Psychiatric Seminar	Wayne State University College of Medicine 1401 Rivard Detroit 7 course at Detroit Receiving Hospital Detroit 26	G Lim 10	II	PD LC Clin C O	6	10/14/60 2/24/61	1/20/61	I 4 sessions 1½ hr monthly Fridays	33 75
Office Psychotherapy for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	G	IC	Lec Pan O AV	15	6/ 1/61	6/ 3/61	C 3 days	40
Readings in Freud	American Institute for Psychoanalysis 329 E 62nd St, New York 21	B Lim 30	II	Sem Lec O	30	9/12/60	2/ 6/61	I 20 sessions 1½ hr weekly Mondays	80
Psychoanalytic Contributions to Psychiatry	American Institute for Psychoanalysis 329 E 62nd St, New York 21	G Lim 20	II	Sem Lec O	22½	9/13/60	12/20/60	I 15 sessions 1½ hr weekly Tuesdays	60
Continuous Case Seminar on the Analytic Relationship	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 20	II	Sem	12	9/19/60	12/ 5/60	I 12 sessions 1½ hr weekly Mondays	60
Seminar in Child Therapy	American Institute for Psychoanalysis 329 E 62nd St New York 21	G Lim 30	II	Sem Lec O	10½	9/23/60	11/ 4/60	I 7 sessions 1½ hr weekly Fridays	28
Our Body Involvement in Emotional Conflict	American Institute for Psychoanalysis 329 E 62nd St New York 21 course at New School for Social Research New York	G Lim 50	II	Sem Lec, O	22½	9/26/60	1/16/61	I 15 sessions 1½ hr weekly, Mondays	30
Psychoanalytic Workshop on Human Behavior	American Institute for Psychoanalysis 329 E 62nd St New York 21 course at New School for Social Research New York	G Lim 30	II	Sem Lec O	22½	9/27/60	1/17/61	I 15 sessions 1½ hr weekly Tuesdays	30
Clinical Conferences on Case Histories I	American Institute for Psychoanalysis 329 E 62nd St New York 21	G Lim 15	II	Sem	15	11/11/60	1/20/61	I 10 sessions 1½ hr weekly Fridays	40
Clinical Conferences	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 10	II	Clin O	15	1/ 9/61	3/13/61	I 10 sessions 1½ hr weekly Mondays	[illegible]
Theory of Neurosis	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 20	II	Sem Lec O	18	1/10/61	3/28/61	I 12 sessions 1½ hr weekly Tuesdays	[illegible]
Problems in Therapy—Post Graduate Course	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 10	II	Sem	15	1/13/61	3/17/61	I 10 sessions 1½ hr weekly Fridays	[illegible]
Workshop on Dreams	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 10	II	Sem	[illegible]	1/13/61	3/17/61	I 10 sessions 1½ hr weekly Fridays	[illegible]
Clinical Conferences on Case Histories II	American Institute for Psychoanalysis 329 E 62nd St New York 21	S Lim 10	II	Sem	[illegible]	[illegible]	[illegible]	I 10 sessions 1½ hr weekly [illegible]	[illegible]

Contemporary Plays and Novels in the Light of Modern Psychoanalysis	American Institute for Psychoanalysis 329 E 62nd St New York 21 course at New School for Social Research New York	C Lim 100	II	Sem Lec O	22½	2/ 2/61	/ 3/61	I 15 sessions 1½ hr weekly Tuesdays	80
Neuroses and Psychoses	American Institute for Psychoanalysis 329 E 62nd St New York 21 course at New School for Social Research New York	G Lim 60	II	Sem Lec O	22½	/ 6/61	/29/61	I 15 sessions 1½ hr weekly Mondays	70
Group Psychodynamics and Group Psychoanalysis	American Institute for Psychoanalysis 329 E 62nd St New York 21 course at New School for Social Research New York	G Lim 60	II	Sem Lec O	22½	2/ 7/61	5/23/61	I 15 sessions 1½ hr weekly Tuesdays	80
Readings in Psychoanalytic Pioneers	American Institute for Psychoanalysis 329 E 62nd St New York 21	G Lim 30	II	Sem Lec O	22½	2/13/61	5/29/61	I 15 sessions 1½ hr weekly Mondays	60
Psychiatric Problems in Medical Practice	The New York Academy of Medicine 2 E 103rd St New York 29	G	II	Sem O	96	Fall 1960		I 48 sessions 2 hr each days unknown	Nil
Family Diagnosis and Family Treatment—Psychiatric Diagnosis and Treatment	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	9	9/28/60	11/ 2/60	I 6 sessions 1½ hr weekly Wednesdays	30
Readings in Psychoanalytic Literature Part I—Freud's Writings up to 1920	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	22½	10/ 4/60	4/25/61	I 15 sessions 1½ hr alternate Tuesdays	60
Psychoanalysis in Groups	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	15	10/ 6/60	12/15/60	I 10 sessions 1½ hr weekly Thursdays	40
Psychosomatic Medicine—Psychoanalytically Oriented	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	12	10/11/60	1/17/61	I 8 sessions 1½ hr alternate Tuesdays	15
Personality Structure and Psychoanalysis	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	15	10/18/60	2/21/61	I 10 sessions 1½ hr alternate Tuesdays	40
Readings in Psychoanalytic Literature Part II—Freud's Writings After 1920 Writings of Other Psychoanalytic Leaders	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	22½	10/18/60	5/ 2/61	I 15 sessions 1½ hr alternate Tuesdays	60
Readings in Psychoanalytic Literature Part II—Works of Reich Sullivan Silverberg Kardiner and Horney	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	9	10/31/60	1/23/61	I 6 sessions 1½ hr alternate Mondays	25
Introductory Lectures in Child Psychiatry	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	II	Lec O	15	1/ 5/61	3/ 9/61	I 10 sessions 1½ hr weekly Thursdays	Unknown
803 The Development of Psychoanalytic Thinking	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Lec	24	9/26/60 2/ 6/61 (Course 803)	1/20/61	I 16 sessions 1½ hr weekly Mondays	75
818 Clinical Conference on Treatment Planning	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Sem	24	9/27/60	1/17/61	I 16 sessions 1½ hr weekly Tuesdays	75
Comprehensive Curriculum in Group Psychotherapy	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 15	II	LC Sem	138	9/27/60	6/ 2/61	I 44 sessions 1½ hr weekly Tuesdays	400
817 Clinical Conference	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Clin O	15	9/28/60	1/18/61	I 10 sessions 1½ hr weekly Wednesdays	60
8 Clinical Conferences	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Clin C	7½	9/28/60 2/ 8/61 (Course 831)	10/26/60	I 5 sessions 1½ hr weekly Wednesdays	40
1 Introduction to Psychotherapy and Psychotherapeutic Techniques	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Lec	18	9/28/60	12/14/60	I 12 sessions 1½ hr weekly Wednesdays	75
80 Techniques of Dream Interpretation	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Sem	22½	9/29/60	1/19/61	I 15 sessions 1½ hr weekly Thursdays	75
817 Clinical Conference Character Disorders	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Clin C	15	2/ 6/61	4/17/61	I 10 sessions 1½ hr weekly Mondays	60
818 The Borderline Patient	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 25	II	LC Sem	15	2/ 8/61	4/26/61	I 10 sessions 1½ hr weekly Wednesdays	60
808 Dream Interpretation Advanced Seminar	Postgraduate Center for Psychotherapy 218 E 70th St New York	S Lim 20	II	Unknown	15	3/22/61	5/31/61	I 10 sessions 1½ hr weekly Wednesdays	75

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PSYCHIATRY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Letchworth Village Graduate Course in Mental Retardation	Research Foundation for Mental Hygiene Letchworth Village, Thiells, N Y	S Lim 12	PT	PD LC BR, Clin C Sem Lec, O, AV, EPP	120	9/19/60 10/ 7/60 3/13/61 4/10/61	10/ 7/60	17 days	Nil
Common Problems of Medical Practice	Hahnemann Medical College 235 N 15th St, Philadelphia	G Lim 40	II	Sem Lec O AV	12	10/20/60	12/ 8/60	I 8 sessions 1½ hr weekly Thursdays	15
Medical Hypnosis	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	B Lim 24	II	PD Clin C Sem Lec Pan O	36	10/ 5/60	4/19/61	I 18 sessions 3 hr weekly Wednesdays	250
Psychotherapy for Physicians	Staunton Clinic, Department of Psychiatry University of Pittsburgh 3601 Fifth Ave, Pittsburgh 13	G Lim 36	II	Sem O EPP	26	9/21/60 1/11/61	12/14/60	I 13 sessions 2 hr weekly Wednesdays, Thursdays	75
Psychiatry	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St, Memphis, Tenn	G Lim 20	IC	PD Sem Lec Pan, O AV, EPP	23	5/24/61	5/26/61	C 3 days	55
Clinical Psychiatry—Part I	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston, Texas course at Memorial Hospital, Houston Texas	G Lim 20 (Both Groups)	II	Sem, Lec	30	Group A 9/ 1/60 Group B 9/ 6/60	Group A 12/15/60 Group B 12/13/60	I 15 sessions (Each Group) 2 hr Tuesdays or Thursdays	60
Principles of Psychiatry for Physicians	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas	G Lim 10	II	Sem O	16	10/ 8/60	10/30/60	I 8 sessions 2 hr twice weekly Saturdays Sundays	30
Clinical Psychiatry—Part II	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg, Texas Medical Center Houston Texas course at Memorial Hospital Houston, Texas	G Lim 20 (Both Groups)	II	Sem Lec	32	Group A 1/24/61 Group B 1/26/61	Group A 5/ 9/61 Group B 5/11/61	I 16 sessions (Each Group) 2 hr Tuesdays or Thursdays	60
Practical Psychiatry	University of Washington School of Medicine Seattle	B Lim 12	IC	PD LC, BR Sem Lec, O AV	Unknown	7/61	Unknown	C 5 days	50

PUBLIC HEALTH AND PREVENTIVE MEDICINE

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Preventive Medicine and Public Health 100	Yale University School of Medicine 333 Cedar St, New Haven, Conn	G	II	Lec AV	25	9/10/60	4/15/61	I 25 sessions 1 hr weekly Saturdays	Nil
Clinical Epidemiology 102	Yale University School of Medicine 333 Cedar St, New Haven Conn	G	II	Sem, Lec, O AV	12	11/29/60	2/28/61	I 12 sessions 1 hr weekly, Tuesdays	Nil
Public Health 103b—Biostatistics Applied to Medicine	Yale University School of Medicine 333 Cedar St, New Haven, Conn	G	II	Lec, O AV	16	2/ 2/61	4/ 6/61	I 8 sessions 2 hr weekly	Nil
Clinical Traineeship in Public Health and Preventive Medicine	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B Lim 2	PT	Sem Lec, O, AV	Unknown	Arranged	Unknown	Unknown	50 mo Kansas residents, 100 mo non residents
Extension Course in Public Health Qualifying for Grade II Local Health Officer in New York State	New York State Department of Health 84 Holland Ave, Albany 8, N Y	G	II and HS	Sem, Lec O, AV	30	Any Time	One year later	Unknown	25
Continuation Education Institutes for Professional Personnel in Public Health	Continuation Education Program Columbia University School of Public Health and Administrative Medicine 600 W 168th St New York 32 Location of course not selected	S Lim 36	IC	Sem Lec		Unknown Repeated		C 2 to 5 days	20 a day
Health Services in the Greater Cincinnati Area	College of Medicine University of Cincinnati Eden and Bethesda Avenues Cincinnati course at Southwestern Ohio Society of General Practice Cincinnati	G	PT	Sem Lec Pan, O, AV	5	10/ 9/60	10/ 9/60	1 day	12

RADIOISOTOPES
(See also Radiology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Radioisotopes in Medicine and Biology	University of Alabama Medical Center Radioisotope Service Birmingham Veterans Administration Hospital Birmingham Ala	S Lim 1[illegible]	II 8 wk IC 1 wk	Lab LD Lec AV EPP	[illegible]	1/12/61	3/10/61	I and C 8 sessions 1½ hr weekly Thursdays [illegible]	[illegible]

Principles and Clinical Uses of Radioisotopes	Continuing Education in Medicine and the Health Sciences University of California Medical Center Second and Parnassus San Francisco	B	IC	Lab PD LC BR Clin C Sem O FPP	180	Arranged	Unknown	C 3 mo	350
Radiology 301—Radioactivity	Yale University School of Medicine 333 Cedar St New Haven Conn	S Lim 10	II	Lab O FPP	36	3/ 9/61	5/25/61	I 12 sessions 3 hr weekly Thursdays	1 0
The Clinical Uses of Radioisotopes	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 24	IC	Lab PD LC Clin C Sem Lec O AV FPP	60	10/ 3/60 3/20/61	10/14/60	C 10 days	200
Clinical Use of Radioisotopes	The University of Michigan Medical Center Department of Postgraduate Medicine 1010 University Hospital Ann Arbor Mich	S	IC	Lab LC BR	40 160	Arranged	Arranged	C 5 20 days	50 wk
Medical Uses of Radioactive Isotopes	Queens Hospital Center 8268 164th St Jamaica 32 N Y	S Rad Lim 20	II	Lab PD LC Clin C Sem Lec Pan O FPP	90	2/ 7/61	6/ 6/61	I 17 sessions 5 hr weekly Tuesdays	275
Radiology PM 3—Use of Radioactive Iodine	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 2	II	Lab PD LC Sem O AV	144	9/60 12/60 3/61	11/60	I 48 sessions 3 hr four times weekly Mondays Tuesdays Thursdays Fridays	300
Radiology PM 41—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	II	Lab PD Lec O AV	102	9/26/60	5/29/61	I 34 sessions 3 hr weekly Mondays	300
Radiology PM 40—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S Lim 15	IC	Lab PD Lec O AV	140	6/ 5/61	6/30/61	C 20 days	300
Radioisotopes for Therapeutic Uses	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G	PT	Lab PD LC BR Clin C Sem Lec Pan O EPP		Arranged	4 to 6 wk later	4 to 6 wk	4 wk 150 6 wk 250
Radioisotope Techniques in Diagnosis	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G	PT	Lab PD LC BR Clin C Sem Lec Pan O FPP		Arranged	4 to 6 wk later	4 to 6 wk	4 wk 150 6 wk 250
[illegible] Radioactive Isotopes	New York University Post Graduate Medical School 550 First Ave New York	G Lim 2	IC	Lab PD LC BR Clin C Sem EPP	150	Arranged	1 mo later	C 1 mo	175
[illegible] Radioactive Isotopes	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 1	II	Lab PD LC BR Clin C Pan FPP	102	10/ 5/60	5/24/60	I 34 sessions 3 hr weekly Wednesdays	125
Hematology and Radioisotopes	American College of Physicians 4200 Pine St Philadelphia 4 course at The Ohio State University College of Medicine Columbus Ohio	S	IC	PD Clin C Sem Lec Pan	40	9/19/60	9/23/60	C 5 days	60 members 80 non members
Physical and Medical Aspects of Radioisotope Use	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at M D Anderson Hospital and Tumor Institute Houston Texas	G Lim 12	IC	Lab PD LC Lec Pan FPP	160	1/ 2/61 Annually	1/27/61	C 20 days	200

RADIOLOGY

(See also Anatomy Occupational Medicine Radioisotopes)

Radiological Physics	Continuing Education in Medicine and the Health Sciences University of California Medical Center Second and Parnassus San Francisco	Res	II	Lec O AV FPP	64	9/20/60	Unknown	I 32 sessions schedule unknown	100 or 50 per semester
Radiological Physics	Office of Postgraduate Medical Education University of Colorado Medical Center 4200 E Ninth Ave Denver 20	C	II	Lab Lec FPP	36	9/ 6/60	6/13/61	I 36 sessions 1 hr weekly Tuesdays	10 per 3 mo
Radiology 302—Introduction to X rays and Radioisotopes	Yale University School of Medicine 333 Cedar St New Haven Conn	S	II	Lec O AV	10	10/19/60	11/16/60	I 5 sessions 2 hr weekly Wednesdays	25
Radiology 303—X ray Physics	Yale University School of Medicine 333 Cedar St New Haven Conn	S	II	Lec O AV FPP	20	12/ 1/60	2/16/61	I 10 sessions 2 hr weekly Thursdays	40
Course II—Clinical Radiology	Cook County Graduate School of Medicine 707 S Wood St, Chicago 12	C Lim 6	PT	PD LC Sem O AV FPP	60	Arranged	2 wk later	11 days	70
Course III—X ray Therapy	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 3	PT	PD LC BR Clin C Sem Surg O AV FPP	30 to 240	Arranged	1 2 4 or 8 wk later	6 to 24 days	60 to 300
Course I—Diagnostic Radiology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 12	IC	PD LC Clin C Lec AV FPP	68	10/17/60 4/10/61	10/28/60	C 11 days	125

Key will be found on page 1670

RA LOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Radium Therapy	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 16	IC	Lab PD LC BR Surg Lec O AV, EPP	30	6/ 5/61	6/ 9/61	C 5 days	100
Radiation Physics	Northwestern University Medical School 303 E Chicago Ave Chicago 11	S Radiology Lim 60	II	Lec	36	1/ 9/61	5/ 8/61	I 18 sessions 2 hr once weekly	50 practicing physicians 25 residents
Radiology of the Chest	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7	S	IC	Lec Pan O AV	35	3/13/61	3/17/61	C 5 days	75 35 for a non Indiana University resident
Radiological Physics	University of Kansas School of Medicine 39th and Rainbow Boulevard, Kansas City, Kan	S	II	Lec O AV	20	10/ 9/60	12/11/60	I 10 sessions 2 hr weekly Sundays	30 or 5 for reenrollment
Radiology	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	S	IC	Lec, Pan O AV	21	2/20/61	2/22/61	C, 3 days	45
Radiographic Diagnosis	Maine Medical Center 22 Bramhall St, Portland Maine	G	PT	Sem Lec O	40	9/60 9/61	6/61	40 days	Nil
General Radiology 1	Harvard Medical School 25 Shattuck St, Boston course at Peter Bent Brigham Hospital, Boston	S Lim 2	IC	PD, LC Clin C Sem O AV, EPP	120 to 130 a mo	Arranged	Arranged	C 26 days a mo	150 a mo
Radiology, Diagnostic	The University of Michigan Medical Center Department of Postgraduate Medicine 1610 University Hospital, Ann Arbor Mich	G Lim 40	IC	Lab, Lec, O, AV	18	4/ 3/61	4/ 5/61	C 3 days	40
Instructional Courses American Roentgen Ray Society	American Roentgen Ray Society 412 Union St, S E Minneapolis 14 course at Ambassador Hotel Atlantic City, N J	S Rad Lim 900	II	Lec, Pan, O, AV	6	9/27/60	9/30/60	I 1½ hr daily	Unknown
Radiology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14 course at Center for Continuation Study, Minneapolis	S Lim 300	IC	Sem, Lec, Pan, O, AV	30	10/31/60	11/ 4/60	C, 5 days	100
Radiological Angiography	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark, N J	G Lim 35	II	Lec O AV	12	10/14/60	12/ 2/60	I 8 sessions 1½ hr weekly Fridays	50
Operative Radium Therapy	Queens Hospital Center 82 68 164th St, Jamaica 32, N Y	S Rad Lim 10	II	Lab, PD, LC, Clin C Sem Surg, Lec, Pan, O, EPP	24	10/ 5/60	11/30/60	I 8 sessions 3 hr weekly Wednesdays	100
Special Radiation Procedures in Treatment of Cancer	Queens Hospital Center 82 68 164th St Jamaica 32, N Y	S Rad Lim 12	IC	Lab PD, LC, Clin C Sem Surg Lec Pan, O, EPP	35	10/17/60	10/21/60	C 5 days	150
Radiology PM 51—Radiotherapy	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	IC	Lab LC, Lec O EPP	6 or 12 mo full time	Arranged	6 or 12 mo later	C 6 or 12 mo	300
Radiology PM 31—Radiology of the Chest	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32 course at Mount Sinai Hospital New York 29	B	IC	Lec, O, AV	10½	9/26/60	10/ 4/60	C 7 days	50
Radiology PM 36—Differential Diagnosis in Gastrointestinal Radiology	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32 course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	10	10/11/60 3/28/61	12/13/60	I 10 sessions 1 hr weekly Tuesdays	50
Radiology PM 31—Differential Diagnosis in Radiology of the Chest	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	G Lim 3	II	PD, LC, Sem	15	10/24/60 3/13/61	1/30/61	I 10 sessions 1½ hr weekly, Mondays	50
Radiology PM 1—Radiologic Physics	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S	II	Lec O AV	36	1/ 3/61	5/ 4/61	I 30 sessions 1 hr twice weekly Tuesdays Thursdays	50

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Radiology PM 80—Roentgenographic Interpretation of Diseases of the Bones and Joints	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Hospital for Joint Diseases New York 35	S	II	Lec O AV	24	3/ 8/61	5/24/61	I 12 sessions 2 hr weekly Wednesdays	150
Radiology PM 32—Roentgen Diagnosis of Lesions of the Gastrointestinal Tract Gall Bladder and Pancreas	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	IC	Lec O AV	10½	3/13/61	3/21/61	C 7 days	50
Radiology PM 2—Neuro radiology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S	IC	PD Lec Pan O AV	37½	4/10/61	4/14/61	C 5 days	100
Radiology PM 33—Radium Therapy	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	II	Lec O AV	12	5/ 9/61	6/20/61	I 6 sessions 2 hr weekly Tuesdays	50
Radiology PM 52—Megavoltage Therapy	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Mount Sinai Hospital New York 29	S	II	Lec O AV	12	5/18/61	6/22/61	I 6 sessions 2 hr weekly Thursdays	50
Roentgen Diagnosis in Gastroenterology	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Beth El Hospital Brooklyn N Y	G Lim 15	II	Lec	8	10/60	12/60	I 8 sessions 1 hr each days unknown	20
X Ray Diagnosis of Chest Diseases	Joint Committee on Post Graduate Education 1313 Bedford Ave Brooklyn N Y course at Beth El Hospital Brooklyn N Y	G Lim 25	II	Lec O	8	4/61	5/61	I 8 sessions 1 hr each days unknown	20
Radium and Roentgen Therapy	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	S	PT	PD LC BR Clin C Sem Surg Lec Pan O EPP		Arranged	4 to 6 wk later	4 to 6 wk	4 wk 150 6 wk 250
Radiation Physics and Protection	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G	PT	Lab PD LC Clin C Sem Lec Pan O EPP		Arranged	4 to 6 wk later	4 to 6 wk	4 wk 150 6 wk 250
Diagnostic Roentgenology	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York	G	PT	Lab PD LC BR Clin C Sem Lec Pan O EPP		Arranged	4 to 6 wk later	4 to 6 wk	4 wk 150 6 wk 250
Radiology	New York Polyclinic Hospital 345 W 50th St New York 19	G Lim 10	IC	Lab LC Clin C Lec EPP	1260	10/ 1/60 4/ 1/61	6/30/61	C 180 days	1000
651—Diagnostic Radiology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 50	II	Lec AV	56	9/21/60	4/26/61	I 28 sessions 2 hr weekly Wednesdays	125
653—Clinical Radiation Therapy	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 2	II	PD LC BR Lec O EPP	54	9/28/60	1/25/61	I 18 sessions 3 hr weekly Wednesdays	100
[illegible]—Radiobiology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 20	II	Sem Lec AV	34	2/ 1/61	5/24/61	I 17 sessions 2 hr weekly Wednesdays	70
Postgraduate Course in Radiology	Cincinnati General Hospital Burnet Ave Cincinnati	S Lim 30	IC	Lab Clin C Lec Pan O AV	40	6/ 5/61 Annually	6/ 9/61	C 5 days	150
Radiologic Physics	Hahnemann Medical College and Hospital 230 N Broad St Philadelphia 2	S Lim 100	II	Lec O	[illegible]	9/27/60 Annually	5/ 9/61	I 32 sessions 1½ hr weekly Tuesdays	Nil
Radiologic Physics Radiobiology Radiology Laboratory Introduction to Isotopes	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	S Lim 20	II	Lab Clin C Lec O	150	9/20/60	1/19/61	I Unknown	150
Radiology	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 4	PT	Lab, Clin C Lec Pan O AV EPP	40	10/10/60	10/14/60	5 days	65
Radiation Beam and Radium Physics	The University of Texas Postgraduate School of Medicine 110 Jesse Jones Library Bldg Texas Medical Center Houston Texas course at M D Anderson Hospital and Tumor Institute Houston Texas	G and Residents	IC	Lab Sem Lec EPP	160	2/ 6/61	3/ 3/61	C 20 days	200

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SURGERY

(See also Anatomy, Pathology, Psychiatry)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Surgery	Continuing Education in Medicine and the Health Sciences University of California San Francisco Second and Parnassus, San Francisco course at Franklin Hospital San Francisco	S	IC	Sem Surg Lec Pan O, AV	11	10/ 8/60	10/ 9/60	C, 2 days	Unknown
Symposium Early Care of the Acutely Injured Patient	University of California Hospital Third and Parnassus San Francisco course at Franklin Hospital San Francisco	G	IC	PD Clin C Lec Pan O AV EPP	10	10 8/60	10/ 9/60	C 2 days	Unknown
Symposium on Current Surgical Practices	Walter Reed Army Institute of Research Walter Reed Army Medical Center Washington 12 D C	S Lim 100	IC	PD Clin C Sem Lec, O, TV EPP	20	1/11/61	1/13/61	C 3 days	Nil
Seminar in Gastrointestinal Surgery	University of Florida College of Medicine Gainesville Florida	B	IC	Clin C Sem Lec, Pan, O	15	Mid 1/61	Unknown	C 2½ days	25
Pediatric Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 16	IC	Lab PD LC BR Surg Lec AV EPP	35	9/19/60 4/24/61	9 23/60	C Unknown	150
Surgery of Colon and Rectum	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 18	IC	Lab, PD LC BR Surg, Lec AV TV EPP	35	9/19/60 11/28/60 3/ 6/61 5/ 1/61 6/19/61	9/23/60	C 5 days	125
One Week Course in General Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 20	IC	PD LC Sem Surg Lec O AV EPP	25	9/19/60 11/28/60 3/ 6/61 5/ 1/61 6/19/61	9 23/60	C, 5 days	150
Course I—Surgical Technic	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 20	IC	Lab PD LC BR Clin C, Surg Lec AV, TV EPP	86	9/26/60 11/ 7/60 12/ 5/60 2/ 6/61 2/27/61 3/13/61 4/17/61 5/16/61 7/10/61 8/ 7/61	10/ 7/60	C 11 days	250
Vaginal Approach to Pelvic Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 16	IC	PD LC BR Surg Lec, AV TV, EPP	20	9/26/60 10/23/60 1/30/61 3/20/61 6/26/61 7/17/61	10/ 7/60	C 5 days	125
Surgery of the Hand	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 16	IC	Lab, PD, LC BR Surg, Lec AV TV, EPP	37	9/26/60 4/17/61	9/30/60	C 5 days	150
Head, Neck and Plastic Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 24	IC	Lab PD, LC BR Surg, Lec AV TV EPP	40	10/ 3/60 12/ 5/60 3/ 6/61 4/10/61	10/ 7/60	C, 5 days	150
Thoracic Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 18	IC	Lab PD, LC, BR Surg, Lec AV TV EPP	30	10/17/60 6/19/61	10/21/60	C, 5 days	150
Gallbladder Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 16	IC	PD LC Sem Surg Lec, O AV EPP	12	10/17/60 4/17/61 6/19/61	10/19/60	C 3 days	80
Surgery of Hernia	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 16	IC	Lab PD, LC BR Surg Lec AV EPP	13	10/20/60 4/20/61 6/22/61	10/22/60	C 3 days	80
Basic Principles in General Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 50	IC	Lab LC Surg, Lec AV, TV	80	10/24/60 4/ 3/61 7/24/61	11/ 4/60	C 11 days	150
Annual Postgraduate Course of the International College of Surgeons	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 50	IC	Lab LC Surg, Lec AV, TV	80	10/24/60 4/ 3/61 7/21/61	11/ 4/60	C 11 days	150
Course III—Fractures and Traumatic Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 20	IC	Lab PD LC BR Surg Lec O AV TV EPP	80	10/24/60 3/ 6/61 6/ 5/61	11/ 4/60	C 11 days	150
General Surgery—Board Review Part I	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 40	IC	Lab Sem Lec O AV TV	110	11/ 7/60	11/19/60	C 12 days	250
Blood Vessel Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 1-	S Lim 40	IC	Lab PD LC Clin C Surg Lec AV TV EPP	37	11/28/60 / 8/61	12/ 2/60	C 7 days	150
			IC	Lab PD LC BR Surg	70	1-/ /60 / 3/61	1-/16/60	C 11 days	0

Breast and Thyroid Surgery	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	G Lim 18	IC	AV TV TTT		7/22/61			
General Surgery—Board Review Part II	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	S Lim 40	IC	Lab Sem Lec O AV TV	110	/15/61 9/ 7/61	/ 7/61	C 12 days	50
Surgery—Pre Operative Evaluation and Post Operative Care of Surgical Patient	Indiana University School of Medicine 1100 W Michigan St Indianapolis	G	IC	Lec Pan O AV	7	4/ 5/61	4/ 5/61	C 1 day	10
Surgery	State University of Iowa College of Medicine University Hospitals Iowa City	G	IC	Sem Pan O AV	12	12/ 6/60	12/ 7/60	C 2 days	[illegible]
Surgery	University of Kansas School of Medicine 39th and Rainbow Boulevard Kansas City Kan	B	IC	PD Lec Pan O AV	25	5/15/61	5/18/61	C 4 days	60
Surgery of the Foot	Tulane University School of Medicine 1430 Tulane Ave New Orleans	S Lim 50	IO	PD Lec Pan O AV	20	2/16/61	2/18/61	C 2½ days	25
General Surgery I	Harvard Medical School 25 Shattuck St Boston course at Massachusetts General Hospital Boston	S	IC	LC Clin C Sem Lec AV	132	10/17/60 6/ 5/61	11/ 4/60	C 17 days	250
Surgical Seminar	Wayne State University College of Medicine 1401 Rivard Detroit 7	S Lim 50	II	Sem	40	10/ 1/60	5/30/61	I 40 sessions 1 hr weekly Mondays	22 50
Surgery for Surgeons	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	S	IC	Surg Lec Pan O AV	15	2/ 9/61	2/11/61	C 3 days	40
Sixth Annual Trauma Day	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G	IO	LC BR Sem Lec Pan O AV	6	5/ 3/61	5/ 3/61	C 1 day	15
Surgery Traineeship for the General Physician	University of Nebraska College of Medicine 42nd and Dewey Omaha 5	G Lim 3	PT	PD LO BR Clin C Sem Surg Lec Pan O AV EPP	15	6/12/61	6/17/61	5½ days	75
Experimental Genito-urinary Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J	S Lim 15	II	Lab Surg O AV EPP	9	10/15/60	10/29/60	I 3 sessions 3 hr weekly Saturdays	60
Experimental Pelvic Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark N J	S Lim 15	II	Lab Surg Lec O AV EPP	9	10/29/60	11/12/60	I 3 sessions 3 hr weekly Saturdays	60
Recent Advances in Clinical Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at United Hospitals of Newark Presbyterian Hospital Unit Newark N J	G Lim 45	II	Lec O AV	15	11/ 3/60	1/19/61	I 10 sessions 1½ hr weekly Thursdays	50
Plastic Surgery of Interest to General Surgeons	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at St Barnabas Medical Center Newark 2 N J	S Lim 15	II	Lec O AV	12	11/ 9/60	1/ 4/61	I 8 sessions 1½ hr weekly Wednesdays	40
One Day Postgraduate Seminar in Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Helen Fuld Hospital Trenton N J	G Lim 45	IO	Lec Pan O AV	4	1/12/61	1/12/61	C 1 day	25
Experimental Vascular Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark N J	S Lim 15	II	Lab Lec O AV EPP	33	1/11/61	3/25/61	I 11 sessions 3 hr weekly Saturdays	220
Experimental Gastro-intestinal Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St Newark 2 N J course at Martland Medical Center Newark N J	S Lim 15	II	Surg Lec O AV EPP	15	4/ 1/61	4/29/61	I 5 sessions 3 hr weekly Saturdays	100
Medicine I M 6, A—Advanced Course in Peripheral Vascular Surgery	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Montefiore Hospital New York 67	S Lim 15	II	Lab PD BR Clin C Surg Lec O AV EPP	54	11/16/60	3/29/61	I 18 sessions 3 hr weekly Wednesdays	150

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SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Laryngo Broncho Esophagology Gastrology	New York Polyclinic Hospital 345 W 50th St, New York 19	S Lim 5	II	Sem Lec Pan, O	26	10/ 5/60 4/ 5/61	11/16/60	I 6 sessions days unknown	75
661—Endocrinologic Aspects of Surgery	New York University Post Graduate Medical School 550 First Ave New York 16	G	IC	Sem Lec Pan AV	21	Unknown		C 3 days	75
551—The Intervertebral Disc	New York University Post Graduate Medical School 550 First Ave New York 16	S Neuro surg Lim 6	IC	PD BR Clin C Lec AV LPP	11	10/ 6/60	10/ 7/60	C 2 days	50
662—Surgery of the Hand	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 20	IC	PD IC Clin C Sem Surg Lec AV LPP	42	2/61		C 6 days	125
663—Pediatric Surgery	New York University Post Graduate Medical School 550 First Ave New York 16	G	IC	Sem Lec AV	21	Spring 1961		C 3 days	75
Seminar on Heterologous Transplantation of Human Tumors and Other Tissues	Sloan Kettering Institute 410 E 68th St New York course at Memorial Center for Cancer and Allied Diseases New York	S Lim 10	IC	Lab Sem Lec Pan O AV LPP	25	10/ 4/60 3/ 7/61	10/ 6/60	C 3 days	Nil
Minor Surgery and Orthopedics	Rochester General Hospital Northside 1125 Portland Ave Rochester N Y	G Lim 50	IC	PD IC BR Lec Pan O AV	5	10/ 6/60	10/ 6/60	C 1 day	10
Surgical Diagnosis and Management	Southwestern Ohio Society of General Physicians 1710 Section Rd Cincinnati 37 course at University of Cincinnati College of Medicine Cincinnati	G	IC	Sem Lec Pan O AV	4	4/ 9/61	4/ 9/61	C 1 day	10
Upper Gastrointestinal Surgery	Frank E Bunts Educational Institute 2020 E 93rd St Cleveland	B Lim 125	IC	PD Clin C Lec Pan O AV	12	1/11/61	1/12/61	C 2 days	30
Bronchology Esophagology and Laryngeal Surgery	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg Philadelphia	S Lim 10	IC	Lab Lec O		6/ 5/61	6/17/61	C 12 days	250
Pre and Postoperative Treatment	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at The Turner Home El Paso, Texas	G Lim 60	IC	Lec AV	7	9/18/60	9/18/60	C 1 day	10
Industrial Surgery	The University of Texas Postgraduate School of Medicine 410 Jesse Jones Library Bldg Texas Medical Center Houston 25 Texas course at The Turner Home, El Paso, Texas	G Lim 60	IC	Lec O AV	7	11/20/60	11/20/60	C 1 day	10
Surgical and Orthopedic Aspects of Trauma	Brooke General Hospital Brooke Army Medical Center Ft Sam Houston Texas	B Lim 100	IC	Lab PD LC, Clin C Sem Lec Pan, O AV	35	3/13/61	3/17/61	C 5 days	Nil
General Practice 1960—Surgery and Its Specialties	University of Wisconsin Medical School 418 N Randall Ave Madison 6 Wis course at Wisconsin Center Building, Madison 6, Wis	G	IC	PD Clin C Sem Lec Pan O AV IV FPP	17½	10/ 6/60	10/ 8/60	C 2½ days	35

UROLOGY

(See also Anatomy, Infertility Pathology)

Title of Course	Location	Designed For	Type	Methods of Education	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Los Angeles Urologic Research Congress	Tracy O Powell M D 6253 Hollywood Blvd, Hollywood 28 Calif course at Ambassador Hotel Los Angeles	S	IC	Sem Lec Pan O AV	40	11/ 7/60	11/11/60	C 5 days	75
Office Urology	University Extension—University of California Los Angeles University of California Medical Center Los Angeles	B	IC	Sem Lec Pan O AV	12	Unknown	Unknown	C 2 days	10
James C Kimbrough Urological Seminar	Walter Reed General Hospital Walter Reed Army Medical Center Washington 12 D C	S Lim 60	IC	Sem	21	11/ 3/60	11/ 5/60	C 3 days	Nil
Ten Day Practical Course in Cystoscopy	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	C Lim 2	PI	PD IC Surg Lec AV LPP	30	9/19/60 10/ 3/60 11/ 7/60 11/28/60 every 2 wk during 1961	9/30/60	10 days	150
Two Week Intensive Course in Urology	Cook County Graduate School of Medicine 707 S Wood St Chicago 12	[illegible]	IC	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

Office Urology	Indiana University School of Medicine 1100 W Michigan St Indianapolis 7								
Urology	State University of Iowa College of Medicine University Hospitals Iowa City	B	IC	PD LC BR Surg Lec O	8	9/23/60	9/24/60	C 1½ days	70
Urology for Specialist	Continuation Medical Education 1342 Mayo Memorial University of Minnesota Minneapolis 14 course at Center for Continuation Study Minneapolis	S	IC	Lec Pan O AV	1	3/27/61	3/29/61	C 3 days	40
Medical and Surgical Aspects of Urinary Tract Disease	University of Buffalo School of Medicine 3435 Main St Buffalo	G	IC	PD Sem Lec Pan O AV FPP	14	10/19/60	10/20/60	C 2 days	30
Urology PM 1—Urological Pathology	Columbia University College of Physicians and Surgeons 630 W 168th St New York 32 course at Columbia Presbyterian Medical Center New York 32	S Lim 12	II	Lab PD Lec O AV	16	1/ 2/61	1/26/61	I 8 sessions 2 hr twice weekly Mondays Thursdays	100
Urology for the General Practitioner	New York Medical College Flower and Fifth Ave Hospitals Fifth Ave and 106th St New York course at Metropolitan Hospital New York 29	G Lim 15	IC	PD LC BR Clin C EPP	18	3/20/61	3/22/61	C 3 days	30
Retropubic Prostatectomy (Operating Room Demonstrations Lectures)	New York Polyclinic Hospital 345 W 50th St New York 19	S Lim 10	IC	Lab Lec FPP	30	10/ 1/60 4/ 1/61	10/ 6/60	C [illegible] days	100
641 Refresher Course in Basic Urology	New York University Post Graduate Medical School 550 First Ave New York 16	G Lim 12	IC	Lab Lec O FPP	35	1/ 9/61	1/13/61	C 5 days	75
641 Advanced Course in Urology (for Specialists)	New York University Post Graduate Medical School 550 First Ave New York 16	S Lim 16	IC	Lab PD BR Clin C Sem Lec O FPP	42	5/ 1/61	5/ 6/61	C 6 days	200
Recent Advances in Urology	Rochester Regional Hospital Council 154 East Ave Rochester 4 N Y course at University of Rochester Medical Center Rochester 20 N Y	G Lim 25	IC	Lec Pan O AV	12	11/ 3/60	11/ 4/60	C 2 days	30
Urinary Tract Diseases	Postgraduate Department University of Tennessee College of Medicine 62 S Dunlap St Memphis Tenn	G Lim 20	IC	Lab PD LC BR Clin C Lec Pan O AV EPP	23	5/ 3/61	5/ 5/61	C 3 days	[illegible]
Seminar on Urology (for non urologists)	University of Virginia School of Medicine Charlottesville Va	G	IO	PD LC Clin C Sem Lec Pan O	6	12/ 2/60	12/ 2/60	C 1 day	10

Key will be found on page 1670

THE SEWING CIRCLE AND THE OBSTETRICIAN ERROR—The errors of translation and spelling may be illustrated by the word S-E-W-E R which may be pronounced sower or sewer. The somewhat ambitious members of a ladies sewing circle got one of their bosomy dowagers, reputed to have a corner on the club's store of Latin, to find a suitable name for this dignified cadre of socially elite. After some research, letters were exchanged with a university's Classics Department. The group became known as the Cloacina Club, envy of all rival circles. For a season the ladies revelled in this mellifluous and dignified name unaware of the olfactory implication. Then a visiting lecturer, enchanted by the title, inquired of its provenance. He was told. There was consternation. Ladies he said, the trouble is that cloacina may seem to spell sower but actually it spells sewer. The name was changed officially but the memory, abetted by their rivals, still haunts them.

Consider the plight of the enthusiastic professor of obstetrics who wanted a suitable inscription carved over the spotless marble doorway of his lavish new clinic which served rich and poor, married or not. His proper obstetrical mood of laissez faire sent him reeling back through his stock of Hippocratic aphorisms. He recalled the admonition First do no harm, especially suitable in an emporium of obstetrics. He used the Latin form of Primum non nocere' This motto was proudly chiseled in the pristine marble. Only afterwards was it pointed out to him that an equally correct and relevant translation was 'Don't be naughty in the first place —W B Bean, M D, The Natural History of Error, *A M A Archives of Internal Medicine*, February, 1960

GEOGRAPHIC CROSS-REFERENCE

STATE	CATEGORY
ALABAMA	
Birmingham	Radioisotopes
Montgomery	General Medicine
CALIFORNIA	
Auburn	General Medicine
Beverly Hills	Cardiovascular Disease
Chico	General Medicine
Eureka	General Medicine
Lake Arrowhead	Dermatology Internal Medicine Pediatrics
Los Angeles	Clinical Pathology General Medicine Hematology Internal Medicine Ophthalmology Pathology Urology
Martinez	Cardiovascular Disease
Marysville	General Medicine
Napa	General Medicine
Oakland	Internal Medicine
Palm Springs	General Medicine
Palo Alto	Basic Sciences Psychiatry
Pasadena	Anesthesiology
Pebble Beach	General Medicine
Redding	General Medicine
San Diego	Anatomy General Medicine
San Francisco	Anatomy Basic Sciences Cardiovascular Disease Chest Diseases Dermatology General Medicine Gynecology Internal Medicine Occupational Medicine Ophthalmology Otolaryngology Pathology Pediatrics Psychiatry Radioisotopes Radiology Surgery
Santa Ana	Cardiovascular Disease
Santa Barbara	Cardiovascular Disease
Santa Monica	General Medicine
Stockton	General Medicine
Tahoe City	General Medicine
Ukiah	General Medicine
Yosemite	General Medicine
COLORADO	
Denver	Anatomy Cardiovascular Disease Chest Diseases Dermatology Electrocardiography Fractures General Medicine Hematology Internal Medicine Obstetrics and Gynecology Ophthalmology Pathology Pediatrics Physical Medicine and Rehabilitation Radiology
Estes Park	Pediatrics
CONNECTICUT	
Hartford	Anesthesiology
New Haven	Anatomy Basic Sciences Chest Diseases Electrocardiography General Medicine Internal Medicine Neurology and Psychiatry Ophthalmology Pathology Pediatrics Public Health and Preventive Medicine Radioisotopes Radiology
WASHINGTON D C	Allergy Basic Sciences Orthopedic Surgery Pathology Pediatrics Surgery Urology
FLORIDA	
Bal Harbour	Obstetrics and Gynecology Orthopedic Surgery
Gainesville	Fractures Neurology Pediatrics

STATE	CATEGORY
FLORIDA (continued)	
Gainesville (continued)	Surgery
Miami	Pathology
Miami Beach	Cardiovascular Disease
Orlando	Malignant Disease
St Petersburg	Internal Medicine
GEORGIA	
Atlanta	Cardiovascular Disease Clinical Pathology Ophthalmology
Augusta	Fractures Internal Medicine Pediatrics Peripheral Vascular Diseases
Savannah	Cardiovascular Disease
Warm Springs	Physical Medicine and Rehabilitation
ILLINOIS	
Alton	General Medicine
Aurora	General Medicine
Centralia	General Medicine
Chicago	Allergy Anesthesiology Basic Sciences Dermatology Electrocardiography Endocrinology Endoscopy Fractures Gastroenterology General Medicine Gynecology Hematology Internal Medicine Neurology Obstetrics Ophthalmology Orthopedic Surgery Otolaryngology Pathology Pediatrics Peripheral Vascular Diseases Psychiatry Radioisotopes Radiology Surgery Urology
Effingham	General Medicine
Elmhurst	General Medicine
Kankakee	General Medicine
Moline	General Medicine
Oak Park	General Medicine
Ottawa	General Medicine
Peoria	General Medicine
Rockford	General Medicine
Waukegan	General Medicine
Winnetka	Psychiatry
INDIANA	
Indianapolis	Anesthesiology Cardiovascular Disease Chest Diseases Electrocardiography Gastroenterology Hematology Internal Medicine Malignant Disease Obstetrics and Gynecology Orthopedic Surgery Otolaryngology Pediatrics Psychiatry Radiology Surgery Urology
IOWA	
Iowa City	Anesthesiology General Medicine Obstetrics and Gynecology Pediatrics Surgery Urology
KANSAS	
Arkansas City	General Medicine
Chanute	General Medicine
Colby	General Medicine
Concordia	General Medicine
Emporia	General Medicine
Garden City	General Medicine
Great Bend	General Medicine
Hutchinson	General Medicine
Kansas City	Anesthesiology Basic Sciences Cardiovascular Disease Chest Diseases Dermatology Electrocardiography Endocrinology Gastroenterology General Medicine Hematology

STATE	CATEGORY
KANSAS (continued)	
Kansas City (continued)	Internal Medicine
	Neurology
	Obstetrics
	Occupational Medicine
	Ophthalmology
	Orthopedic Surgery
	Otolaryngology
	Pathology
	Pediatrics
	Physical Medicine and Rehabilitation
	Psychiatry
	Public Health and Preventive Medicine
	Radiology
	Surgery
Manhattan	General Medicine
KENTUCKY	
Lexington	General Medicine
Louisville	Cardiovascular Disease
	Chest Diseases
	General Medicine
	Pediatrics
LOUISIANA	
New Orleans	Ephebology
	Internal Medicine
	Malignant Disease
	Otolaryngology
	Pediatrics
	Surgery
Shreveport	General Medicine
MAINE	
Lewiston	General Medicine
	Internal Medicine
Portland	Anesthesiology
	Electrocardiography
	General Medicine
	Radiology
Waterville	Ophthalmology
MARYLAND	
Baltimore	Anatomy
	Basic Sciences
	Cardiovascular Disease
	Internal Medicine
	Occupational Medicine
	Pathology
MASSACHUSETTS	
Boston	Anatomy
	Basic Sciences
	Cardiovascular Disease
	Chest Diseases
	Dermatology
	Electrocardiography
	Ephebology
	General Medicine
	Gynecology
	Hematology
	Internal Medicine
	Neurology
	Obstetrics and Gynecology
	Ophthalmology
	Orthopedic Surgery
	Pediatrics
	Radiology
	Surgery
Brookline	Obstetrics and Gynecology
Holyoke	General Medicine
New Bedford	General Medicine
Northhampton	General Medicine
Westfield	Malignant Disease
MICHIGAN	
Ann Arbor	Allergy
	Anatomy
	Basic Sciences
	Cardiovascular Disease
	Chest Diseases
	Electrocardiography
	Endocrinology
	Fracture
	Gastroenterology
	General Medicine
	Hematology
	Infertility
	Internal Medicine
	Neurology
	Obstetrics and Gynecology
	Ophthalmology
	Otolaryngology
	Pathology
	Pediatrics
	Psychiatry
	Radioisotopes
	Radiology
Detroit	Anatomy
	Anesthesiology
	Basic Science
	Dermatology
	Endocrinology
	Hematology
	Internal Medicine
	Neurology
	Neurology and Psychiatry
	Pathology
	Psychiatry
	Surgery
MICHIGAN (continued)	
Highland Park	Electrocardiography
	Internal Medicine
MINNESOTA	
Minneapolis	Allergy
	Anesthesiology
	Dermatology
	Electrocardiography
	General Medicine
	Gynecology
	Internal Medicine
	Malignant Disease
	Neurology
	Obstetrics
	Ophthalmology
	Orthopedic Surgery
	Otolaryngology
	Pediatrics
	Physical Medicine and Rehabilitation
	Proctology
	Psychiatry
	Radiology
	Surgery
	Urology
Rochester	Ophthalmology
	Otolaryngology
MISSISSIPPI	
Greenwood	General Medicine
Gulfport	General Medicine
Hattiesburg	General Medicine
Jackson	Cardiovascular Disease
	General Medicine
	Malignant Disease
Meridian	General Medicine
Tupelo	General Medicine
MISSOURI	
Kansas City	Cardiovascular Disease
St Joseph	General Medicine
St Louis	Cardiovascular Disease
	Otolaryngology
	Pediatrics
NEBRASKA	
Lincoln	Obstetrics
Omaha	Anesthesiology
	Electrocardiography
	Gastroenterology
	Hematology
	Neurology and Psychiatry
	Obstetrics and Gynecology
	Pediatrics
	Physical Medicine and Rehabilitation
	Surgery
NEW JERSEY	
Atlantic City	General Medicine
	Radiology
Elizabeth	General Medicine
Jersey City	Obstetrics
Long Branch	General Medicine
Montclair	General Medicine
Morristown	Gastroenterology
Neptune	General Medicine
Newark	Basic Sciences
	Cardiovascular Disease
	Electrocardiography
	Endocrinology
	General Medicine
	Internal Medicine
	Malignant Disease
	Occupational Medicine
	Orthopedic Surgery
	Pathology
	Pediatrics
	Radiology
	Surgery
New Brunswick	Internal Medicine
Paterson	Obstetrics and Gynecology
Teaneck	Internal Medicine
Trenton	General Medicine
	Surgery
NEW MEXICO	
Albuquerque	Internal Medicine
Ruidoso	General Medicine
NEW YORK	
Albany	Public Health and Preventive Medicine
Buffalo	Allergy
	Anesthesiology
	Basic Science
	Cardiovascular Disease
	Clinical Pathology
	Electrocardiography
	General Medicine
	Obstetrics and Gynecology
	Orthopedic Surgery
	Otolaryngology
	Pathology
	Pediatrics
	Urology
Flushing	Cardiovascular Disease
	Internal Medicine
Jamaica	Radioisotopes
	Radiology
Kings Park	Neurology

STATE	CATEGORY
NEW YORK (continued)	
New Hyde Park	Pathology
New York	Allergy
	Anatomy
	Anesthesiology
	Basic Sciences
	Cardiovascular Disease
	Chest Diseases
	Clinical Pathology
	Dermatology
	Electrocardiography
	Endocrinology
	Fractures
	Gastroenterology
	General Medicine
	Gynecology
	Hematology
	Infertility
	Internal Medicine
	Malignant Disease
	Neurology
	Neurology and Psychiatry
	Obstetrics
	Obstetrics and Gynecology
	Occupational Medicine
	Ophthalmology
	Orthopedic Surgery
	Otolaryngology
	Pathology
	Pediatrics
	Peripheral Vascular Diseases
	Physical Medicine and Rehabilitation
	Proctology
	Psychiatry
	Public Health and Preventive Medicine
	Radioisotopes
	Radiology
	Surgery
	Urology
Rochester	Electrocardiography
	Gastroenterology
	Internal Medicine
	Obstetrics and Gynecology
	Pediatrics
	Surgery
	Urology
Roslyn	Cardiovascular Disease
Saranac Lake	Chest Diseases
Schenectady	Chest Diseases
Syracuse	Chest Diseases
	Pediatrics
Thiells	Psychiatry
Wards Island	Neurology
Welfare Island	Neurology
NORTH CAROLINA	
Asheville	General Medicine
Chapel Hill	General Medicine
Edenton	General Medicine
Durham	Anesthesiology
	Electrocardiography
Morganton	General Medicine
NORTH DAKOTA	
Grand Forks	General Medicine
OHIO	
Cincinnati	Cardiovascular Disease
	Ophthalmology
	Otolaryngology
	Public Health and Preventive Medicine
	Radiology
	Surgery
Cleveland	Clinical Pathology
	General Medicine
	Internal Medicine
	Ophthalmology
	Physical Medicine and Rehabilitation
	Surgery
Columbus	Chest Diseases
	Hematology
	Internal Medicine
	Occupational Medicine
	Ophthalmology
	Radioisotopes
Toledo	Cardiovascular Disease
OKLAHOMA	
Oklahoma City	Internal Medicine
OREGON	
Portland	Allergy
	Electrocardiography
	Gastroenterology
	Neurology
	Obstetrics and Gynecology
	Ophthalmology
	Orthopedic Surgery
	Otolaryngology
	Pediatrics
PENNSYLVANIA	
Erie	General Medicine
Philadelphia	Anesthesiology
	Basic Sciences
	Cardiovascular Disease
	Chest Diseases
	Dermatology
	Electrocardiography
	Gastroenterology
PENNSYLVANIA (continued)	
Philadelphia (continued)	General Medicine
	Hematology
	Internal Medicine
	Neurology
	Otolaryngology
	Pathology
	Pediatrics
	Peripheral Vascular Diseases
	Psychiatry
	Radiology
	Surgery
Pittsburgh	Allergy
	Anesthesiology
	General Medicine
	Psychiatry
SOUTH CAROLINA	
Charleston	General Medicine
TENNESSEE	
Memphis	Allergy
	Anesthesiology
	Electrocardiography
	Fractures
	Hematology
	Internal Medicine
	Neurology
	Obstetrics and Gynecology
	Pediatrics
	Psychiatry
	Radiology
	Urology
Nashville	General Medicine
TEXAS	
Austin	Pediatrics
Beaumont	Pediatrics
Corpus Christi	Pediatrics
Dallas	Allergy
El Paso	Obstetrics and Gynecology
	Pediatrics
	Surgery
Ft Sam Houston	Obstetrics and Gynecology
	Surgery
Houston	Anatomy
	Anesthesiology
	Basic Sciences
	Cardiovascular Disease
	Dermatology
	Endoscopy
	Fractures
	Hematology
	Infertility
	Internal Medicine
	Malignant Disease
	Ophthalmology
	Pathology
	Pediatrics
	Psychiatry
	Radioisotopes
	Radiology
Hunt	General Medicine
Lubbock	Pediatrics
San Angelo	Pediatrics
San Antonio	Pediatrics
Temple	Anesthesiology
	General Medicine
	Proctology
Texarkana	Pediatrics
Victoria	Electrocardiography
UTAH	
Salt Lake City	Electrocardiography
VIRGINIA	
Charlottesville	Electrocardiography
	Endocrinology
	General Medicine
	Urology
Roanoke	Ophthalmology
WASHINGTON	
Seattle	Basic Sciences
	Cardiovascular Disease
	Chest Diseases
	General Medicine
	Hematology
	Internal Medicine
	Pediatrics
	Psychiatry
WISCONSIN	
Madison	Basic Sciences
	Chest Diseases
	Endocrinology
	Gynecology
	Hematology
	Internal Medicine
	Malignant Disease
	Surgery
Milwaukee	General Medicine
Wauwatosa	Gastroenterology
	Internal Medicine
CANADA	
Montreal Quebec	Pediatrics
Toronto	Internal Medicine
MEXICO	
Mexico City	General Medicine
	Internal Medicine

CLINICAL NOTES

NEURITIS OCCURRING AFTER INSECT STINGS

Norman P Goldstein, M D , C Wilbur Rucker, M D
and
Henry W Woltman, M D , Rochester, Minn

Although allergic reactions to the stings of bees and wasps have been recorded on a number of occasions, these reactions usually were exaggerations of the common local response, urticaria, or a reaction of an anaphylactic type Perlman[1] reviewed the literature and reported seven cases of 'near-fatal allergic reactions to bee and wasp stings "

Less common is the development of neuritis after the sting of an insect Ross[2] reported that allergy to honeybee stings may result in the clinical picture of peripheral neuritis Petechiae may be found in the central nervous system when reaction to the sting of an insect is followed by death[3] Cerebral edema, intraventricular hemorrhage, and meningeal hyperemia also have been reported after death from such a sting[4] Presumably, similar changes may take place in cranial or peripheral nerves, leading to neuritis, although histological evidence for this supposition is lacking

Because of the scarcity of reports of neuritis after insect stings, we believe that the following reports of cases may be of interest and may stimulate the publication of similar material by others interested in this subject At present, it is not commonly appreciated that the sting of an insect occasionally can cause neuritis

Report of Cases

Case 1 —A 30-year-old man registered at the Mayo Clinic on Sept 6, 1952, complaining chiefly of difficulty with vision in the left eye during the previous two weeks The patient's history was essentially noncontributory He said that on Aug 11, 1952, he had been stung by a bee (type not known) on the left temple, after which the left side of his face swelled considerably In about two weeks he noted blurring of vision in the left eye He was referred to the Mayo Clinic by a specialist in diseases of the eye, ear, nose, and throat, the diagnosis was acute optic neuritis of the left eye

Ophthalmoscopic examination revealed the patient s vision to be 6/7 with correction in both eyes The right optic disk was flat and clearly outlined The left optic disk (see figure, *a*) was elevated 1+ diopter Overlying the left optic disk the capillaries were engorged and there were a few small hemorrhages, there were a few other small hemorrhages at the poles The perimetric fields were normal except for enlargement of the left physiological blind spot

Results of the neurological examination were within normal limits, except for the appearance of the left fundus Otorhinolaryngologic examination disclosed no abnormal findings

Results of various laboratory tests, including urinalysis, determination of hemoglobin content, leukocyte count, sedimentation rate, and a serologic test for syphilis, were either normal or negative Roentgenograms of the head showed nothing of significance, and those of the sinuses demonstrated only a slightly thickened membrane in the right antrum The cerebrospinal fluid was of normal pressure and contained 40 mg of protein per 100 cc and one lymphocyte per cubic millimeter, the reaction to the Kolmer test was negative, and the colloidal gold curve was normal The content of sugar and chloride in the cerebrospinal fluid was normal An electroencephalogram disclosed nothing of significance

Examination of the optic fundi on Oct 10 led to the conclusion that the edema of the left optic disk was receding, the elevation was measured as 1 diopter A dark hemorrhage was seen at the nasal margin of the left optic disk Perimetry showed that the left blind spot was smaller and almost within normal limits On Nov 7, examination of the left optic nerve head (see figure, *b*) revealed only a small remnant of the hemorrhage as the sole pathological finding The field of the left eye was normal The diagnosis of papilledema as an allergic manifestation of a bee sting was made

Case 2 —A 52-year-old woman registered at the Mayo Clinic on July 26, 1955, complaining chiefly of numbness of the left arm and left leg that had been present for five or six weeks She said that on June 25 of that year she had been stung by a hornet (type unknown) on the palmar tip of the left middle finger, an average local reaction to the sting then occurred About a week later she noted the onset of numbness in this finger and described it as a "lack-of-touch' sensation with some 'tingling " Within a

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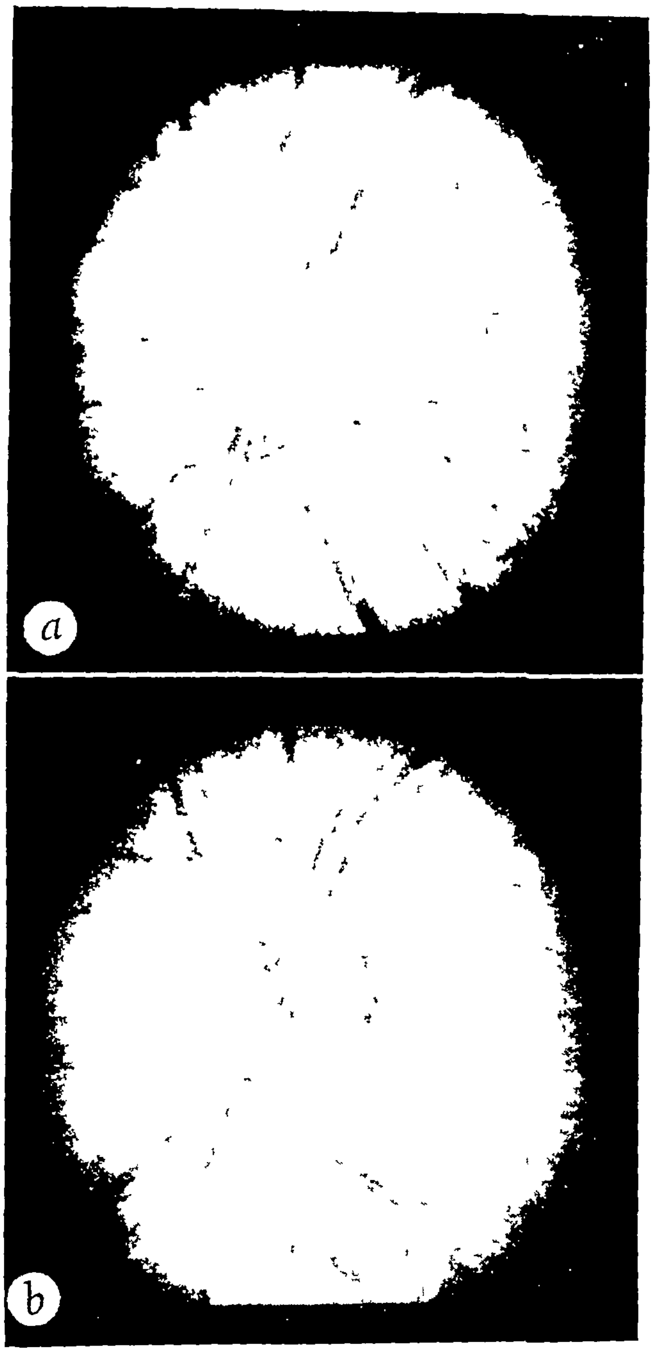
From the sections of neurology and ophthalmology Mayo Clinic and Mayo Foundation Dr Woltman is an emeritus member of the Section of Neurology The Mayo Foundation is a part of the Graduate School of the University of Minnesota day or two the numbness spread to the other fingers of the left hand and then extended proximally up the palmar side of the hand and arm to the left axilla. Within about one week she noted similar paresthesias of the left leg and judged that perhaps she was somewhat clumsy on this leg when walking. The paresthesia in the left leg persisted for only a week, but that in the left *arm became progressively* worse. She also noted that the left hand had become clumsy *when she used it for sewing* and knitting, and often she could not determine what she was touching with the left hand when she was not looking at the object concerned.



Appearance of left optic nerve head of patient in case 1 on (*a*) Sept. 6, 1952, and (*b*) on Nov. 7, 1952.

Results of the general medical examination were essentially normal. Neurological examination revealed only a slight degree of ataxia during tandem walking, although it was noted that she walked with a wide base. The muscle-stretch reflexes in the right arm were normal, whereas the left biceps and brachioradialis reflexes were moderately decreased, and the left triceps reflex seemed normal. In the legs the right quadriceps reflex was slightly more active than the left, and the ankle reflexes were equal and active. Muscle strength appeared to be normal. Results of the sensory examination were normal except for the observations in the left arm; there was a glove type of sensory disturbance to a point above the elbow and subjective decrease in feeling cotton (the patient said, "It feels goofy"), while there were subjective hyperalgesia and increased sensitivity to testing with hot and cold objects. Two-point discrimination was markedly impaired in the fingers of the left hand, and stereognosis was slightly decreased. There was a *slight* decrease in vibratory sensation in both legs at the ankles, but the ability to perceive joint sensation was normal in all four extremities.

Laboratory tests, including urinalysis, determination of hemoglobin content, erythrocyte and leukocyte counts, and a serologic test for syphilis gave either normal or negative results. Gastric analysis revealed the presence of free hydrochloric acid. Roentgenograms of the head disclosed nothing significant, those of the thorax showed only a slight tracheal deviation to the left, and roentgenograms of the cervical part of the spinal column demonstrated nothing but small ossicles in the ligamentum nuchae. The pressure of the cerebrospinal fluid was normal, as was the response to jugular compression. The fluid contained 40 mg. of protein per 100 cc. and one lymphocyte per cubic millimeter; the reaction to the Kolmer test was negative. An electroencephalogram was interpreted as showing only generalized minimal dysrhythmia.

This patient was seen again on Jan. 22, 1957. At that time she said that the difficulty with the left hand had persisted and that she found it awkward to use the hand in buttoning and sewing. The "numbness" had become a "dead feeling," but there were no longer sensations of "pins and needles." Moreover, the paresthesias in the left arm extended only from the fingers to the wrist and had disappeared from the wrist to the axilla. Sensory examination disclosed subjective hypesthesia, hyperalgesia, and thermhyperesthesia over the left hand, but two-point sensation was normal, as was stereognosis. Vibratory sensation was normal over the right ankle and was moderately decreased over the left. The muscle-stretch reflexes were equal and active, except for the left biceps reflex, which was slightly decreased when compared with that on the right side. The patient walked on a somewhat wide base and exhibited slight ataxia on tandem walking. It was noted that the left hand was clumsy when the patient untied and tied her shoelaces and when she tried to unhook her watch band, the wrist watch at this time being worn on the right wrist.

A diagnosis of allergic neuritis of the left upper extremity occurring after the sting of a hornet was made; it was difficult to be sure of the significance of the complaints referable to the left leg.

CASE 3.—A 73-year-old man registered at the Mayo Clinic on Nov. 26, 1957, complaining chiefly of pain in the left side of the face that had been present about 14 months. He said that on Sept. 14, 1956, he had been stung on the margin of the left lower eyelid. He had felt the pain of the sting and thought that probably he had been stung by a spider, although he did not identify the insect with certainty.

Within five minutes the left side of the face swelled to two or three times the normal size, from the left eye down to the left side of the mouth. The left eye became "quite red." For about a month he noted sensations of itching and burning over the left cheek. Then, about a month after the sting of the insect, he noted a constant burning pain in the left cheek in addition to five or six episodes a day of a sharp, shooting pain in the same area when the face was touched in the distribution of the first or second division of the left trigeminal nerve. This sharp, intense pain lasted only a second or two, whereas the sensation of burning was present all day. There was no trigger action and no pain or paresthesia in the distribution of the third division of the left trigeminal nerve. About six weeks before his examination at the Mayo Clinic his physician had injected procaine hydrochloride into the left infraorbital nerve, and this brought about relief of the pain and paresthesias for about three hours.

Results of the general medical examination were essentially normal and neurological examination disclosed nothing of significance except for the sensory findings. There was a minimal but definite decrease in the perception of light touch over the left cheek, and the patient said that touching this area with cotton "makes it burn more." There was also moderate hypalgesia to pinprick over the same area, and he said that, although the pin seemed to be less sharp, "it increases the burning pain." Testing with hot and cold bottles over the left cheek likewise demonstrated a minimal but definite decrease in the perception of temperature.

Results of the usual laboratory tests, including urinalysis, determination of hemoglobin content, erythrocyte and leukocyte counts, differential leukocyte count, determinations of blood urea and fasting blood sugar levels, and a serologic test for syphilis, were either normal or negative. Roentgenograms of the thorax revealed patchy fibrosis and calcification in the fields of the upper and middle portions of the right lung, with compensatory emphysema in the remaining portion of the lung. Specimens of the sputum were cultured for tuberculosis organisms and fungi, but results were negative. Culture of a sample of gastric washings for species of Mycobacterium likewise produced nothing significant. Reaction to a tuberculin test with purified protein derivative (P. P. D.), first and second strength, was negative. Roentgenograms of the head and the sinuses revealed no abnormality, but roentgenologic examination of the colon disclosed diverticulosis.

An alcohol block of the left infraorbital nerve was attempted, but this did not relieve the pain and it was noted that the patient still had perception of pinprick over the left side of the upper lip. Alcohol injection of the second division of the left fifth nerve was attempted the next day, and this produced anesthesia in the distribution of the second division and stopped the pain.

In a letter to us, dated Jan. 23, 1958, the patient wrote that the left facial pain had returned. Our diagnosis was that of left trigeminal neuritis occurring after the sting of an insect, probably a spider.

Comment

Neuritis which occurs after the injection of foreign protein is not uncommon. Various types of neuritis may occur after the administration of vaccines or antitoxin prepared from horse serum. Presumably the neuritis is an "allergic reaction" involving either cranial nerves or, more commonly, the peripheral nervous system. Despite the gaps in our knowledge of "allergic neuritis," it is logical to assume that the neuritis which occurs after the sting of an insect may be similar in pathogenesis to the neuritis which develops after the clinical use of antitoxins or to the experimental neuritis in animals produced by injection of either homologous or heterologous nerve-adjuvant mixtures.[5] The possibility remains that the neuritis in our patients represents a "toxic" rather than an "allergic" neuritis, but our knowledge of the mechanism is too meager to warrant belaboring the semantics involved in the distinction.

Still, it may be important to realize that different insects possess multiple antigens. Foubert and Stier[6] extracted antigenic material from the bodies of wasps, honeybees, black hornets, yellow hornets, and yellow jackets. The individual extracts were injected subcutaneously in rabbits to sensitize the animals. After several weekly injections an Arthus reaction developed in the animals. At this point an alum-precipitated antigenic extract was injected intraperitoneally into the animals. Then the rabbits were bled, and serums with high precipitin titers were prepared. These were tested against the antigenic extracts of the different insects. By this technique it was found that the extracts of the five species of insects each contained four to six antigenic components. Two of these antigenic components seemed to be common to the five species. The other antigenic fractions were specific for each species.

Thus, it can be seen that a sting inflicted by one species of insect may sensitize a patient to the stings of other insects. In none of our three patients was there a history of a previous reaction to an insect sting. However, insect stings which do not cause more than a minor local reaction are sufficiently common to make it possible that these patients had been sensitized in the past. On the other hand the neuritis which occurs after the use of antitoxins prepared from horse serum may develop in patients who were never injected with horse-serum products previously and who had a negative reaction to a skin or conjunctival test when the antitoxin was administered intracutaneously or ophthalmically However, it is appreciated that negative reactions to skin and ophthalmic tests with antitoxin make immediate serum reactions unlikely and that the same reaction to a skin or ophthalmic test provides no information as to the possibility of a delayed serum reaction, with the development of neuritis Perlman[1] wrote that, in his cases of allergic reaction to the stings of bees and wasps, "a positive skin test is not required for proof of an existing allergy," inasmuch as four of his seven patients exhibited a negative reaction to such a test In none of our patients was the skin test used, the potential danger of the procedure under the circumstances at hand seemed to us to outweigh the value of the information which might have been derived from this test

At present, treatment of the neuritis which occurs after the sting of an insect is primarily symptomatic Two of our three patients improved spontaneously, the neuritic pain and paresthesias of the third patient were relieved for several hours by injection of a local anesthetic agent into the involved infraorbital nerve, and later he obtained relief for several months after the injection of alcohol into the maxillary nerve From a theoretical point of view it would be important and interesting to institute therapy with cortisone immediately after the onset of this type of neuritis The local reaction to an insect sting can be treated by the application of an ice bag, a paste of baking soda, antipruritic salves, and the oral use of antihistaminic agents, but it is unlikely that treatment of the local reaction would prevent the subsequent development of neuritis The immediate serum reaction which resembles an experimental anaphylactic reaction in sensitized laboratory animals should be treated by the prompt subcutaneous or intravenous administration of epinephrine If possible, it might be helpful to place a tourniquet proximal to the area of the insect sting The administration of an antihistaminic agent and either cortisone or adrenocorticotropic hormone (ACTH) also might be beneficial

Allergic reactions to the stings of insects raise the question of prophylaxis among certain patients The simplest and most effective prophylaxis is the prevention of additional insect stings When a patient is likely to be the victim of more stings because of his vocation or avocation, the physician should consider the possibility of "desensitization" by the parenteral administration of extracts of these insects[7] Since desensitization to antigens of one species of insect may not protect a person against an allergic reaction to the sting of an insect of another species, it may be necessary to use extracts of several common species of insects, especially when the species of the offending insect cannot be determined with certainty

We did not believe that desensitization with extracts of various insects was indicated in our patients, since prevention of additional insect stings seemed more reasonable, these patients can use insect repellents when they are working in the garden or at picnics or in other situations in which insect stings are common Moreover, we did not know if the injection of even minute amounts of antigen from insects as used in a desensitization program would cause exacerbation of the neuritis It should be noted, however, that none of these three patients had a history of previous allergic reactions, such as pollenosis, bronchial asthma, urticaria, or eczema Furthermore, it is of interest that the neuritis developed in a nerve or nerves adjacent to the site of the insect sting

Summary

In three patients neuritis occurred after the sting of an insect None of the patients was considered to be of an "allergic disposition" In one instance papilledema arose, in the second patient neuritis of an upper extremity developed, and in the third patient neuritis involved the first and second divisions of the trigeminal nerve In each case the involved nerve was in proximity to the location of the insect sting It is postulated that these are examples of an "allergic neuritis," with some similarity to the neuritis of a delayed serum reaction after the administration of an antitoxin Two of the three patients noted spontaneous abatement of the neuritis after a time

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OPTIC AND PERIPHERAL NEURITIS

PROBABLE EFFECT OF PROLONGED CHLORAMPHENICOL THERAPY

Capt Robert J T Joy, Capt Raymond Scalettar
and
Capt Donald B Sodee, (MC), U S Army

Chloramphenicol is one of the most valuable antibiotics available to the physician,[1] although in rare instances it may cause severe hematopoietic reactions [2] It is the purpose of this paper to emphasize another apparent severe toxic reaction—the occurrence of optic and peripheral neuritis

Report of a Case

The patient was a 20-year-old man who had been in good health until Oct 21, 1957, when he was treated with penicillin for a 'flu-like" syndrome Three days later genitourinary symptoms occurred, he became systemically ill and was hospitalized Physical examination at that time showed only costovertebral angle tenderness He had marked pyuria, and his chest roentgenogram showed a small infiltrate in the upper lobe of his left lung He was treated with chlortetracycline and his genitourinary symptoms subsided On Nov 7, pain developed in his left shoulder, but roentgenograms were normal A nonproductive arthrocentesis was performed, with the instillation of penicillin He remained intermittently febrile, with temperatures as high as 103 F (39 4 C) Blood cultures showed Diplococcus pneumoniae, resistant to penicillin and sensitive to chloramphenicol," and he received the latter drug for 10 days without any decrease in his fever He was transferred to Walter Reed General Hospital on Nov 27, 1957

His physical examination on admission revealed only slight tenderness of the left shoulder Three days later an acute septic arthritis of the shoulder joint developed Thick chocolate-colored pus was removed by arthrocentesis and Pseudomonas pseudomallei was isolated in culture and in guinea pigs This established the diagnosis of melioidosis On Dec 11, 1957, in accord with antibiotic sensitivity determinations, treatment was begun with chloramphenicol, 3 Gm daily, novobiocin, 3 Gm daily and sulfisoxazole, 4 Gm daily

Five arthrocenteses were performed at weekly intervals, and the last positive culture was obtained on Dec 21, 1957 Intermittent fever rising to 104 F (40 C) continued during the first week of therapy The patient was afebrile during the rest of his hospital stay In two months his shoulder was asymptomatic and he had regained complete range of motion In January, 1958, his white blood cell count fell to 2,900 per cubic millimeter but returned to normal the next month On March 13, 1958, he began to complain of numbness, tingling, and burning of his feet Examination revealed no position or proprioceptive losses, but hyperesthesia was found over the dorsa of both feet and the anterior aspects of the lower thirds of both legs The peripheral pulses were normal Findings of a lumbar puncture were also normal On March 19 he mentioned blurred vision and an inability to focus while reading Funduscopic examination at this time showed normal findings In spite of the suggestion of drug toxicity, therapy was continued because without long-term antibiotic therapy,[3] there is a danger of fatal relapse in melioidosis

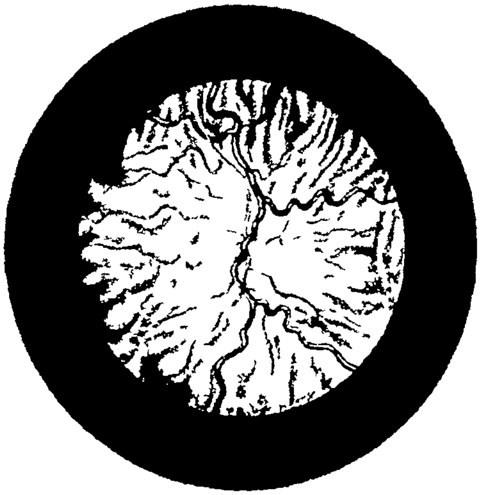

Fig 1 —Artist s conception of appearance of retina during period of acute optic neuritis

On April 1 severe burning sensations developed in the soles of both feet, but there were no changes in the objective neurological findings On April 20 funduscopic examination showed bilateral moderate papillitis, with tortuosity and engorgement of the vessels (fig 1) Visual field examination showed bilateral enlargement of the blind spot and central scotomas measuring 18 degrees on the left and 12 degrees on the right, with an associated diminution of the peripheral visual fields (fig 2)

A diagnosis of toxic optic and peripheral neuritis probably due to chloramphenicol was made Ad-

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From the Department of Medicine Walter Reed General Hospital Walter Reed Army Medical Center Washington 12 D C Captain Joy is now at the U S Army Medical Research Laboratory Fort Knox Kentucky ministration of all antibiotics was discontinued The patient was given vitamin B_{12}, 1,000 mcg, vitamin B complex, and vitamin C, 300 mg, intramuscularly daily for 10 days He then received 100 mg of pyridoxine and six multivitamin capsules daily by mouth, each capsule containing 5,000 USP units of vitamin A, 400 USP units of vitamin D, 75 mg of vitamin C, 2 mg of thiamine, 3 mg of riboflavin, and 20 mg of nicotinamide Visual field examination on May 8 showed a decrease in the size of the blind spots and central scotomas and normal peripheral fields (fig 3) The patient's vision was subjectively normal Oral vitamin therapy was continued until July 23, 1958 His shoulder remained normal and his peripheral neuritis had markedly improved by Sept 2, 1958, when he was returned to duty

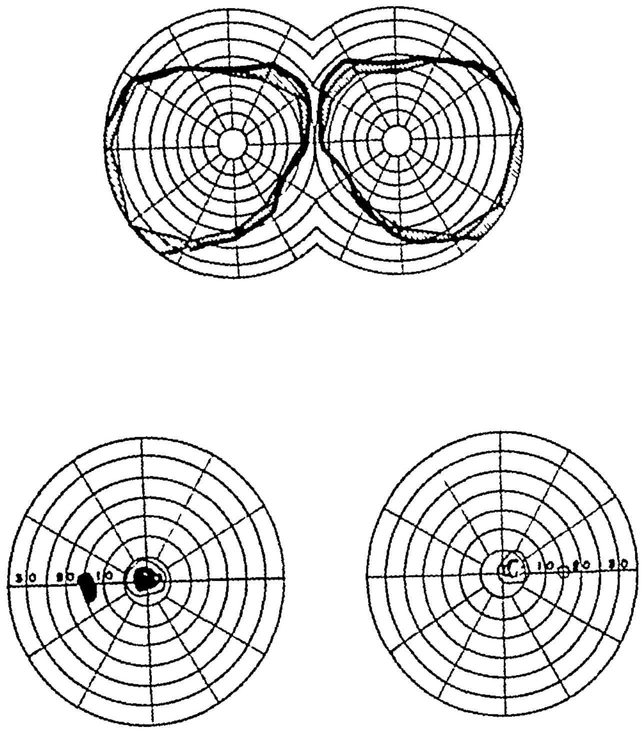

Fig 2 —Visual fields at examination on April 22, 1958, during period of acute optic neuritis

He was examined again in April, 1959 There was no evidence of relapse of the Ps pseudomallei infection He had full use of the left shoulder and had performed full military duty as a bandsman without difficulty He denied having visual symptoms but stated that after prolonged marching his feet tingled and burned Findings of a complete neurological examination were normal Visual fields were unchanged from the examination of May 8, 1958 (fig 3)

Comment

Central nervous system and peripheral neuromuscular toxicity due to chloramphenicol have been previously described[4] Headache,[5] mild depression, "dazed feelings,"[6] internal ophthalmoplegia,[7] and mental confusion and delirium[8] have all been noted in some patients receiving this drug for a variety of infectious diseases It is always difficult, of course, to distinguish side-effects of a drug from the course of the disease being treated[4]

Visual symptoms such as "filmy vision,"[9] "visual disturbance of a few hours' duration,"[5] and "transient visual disturbances"[10] often attributed to ocular muscle palsies[11] have been recorded Since more specific details are lacking in these reports, it is not possible to distinguish ocular myopathy from optic nerve involvement

We have found five additional cases of definite involvement of the optic nerve associated in three instances with peripheral neuritis attributed to chloramphenicol toxicity (see table) Analysis of these cases suggests that these toxic symptoms were related both to large total doses of the drug and to long periods of administration It is always difficult to causally relate a drug and a toxic reaction, particularly if the number of such occurrences is small when compared to the population at risk[12] In the five cases, as well as in ours, there was no other single common denominator of drug or disease Age and sex appear to be unimportant Three of the patients had subacute bacterial endocarditis, with resistant organisms, and two had melioidosis The range of total doses for chloramphenicol was from 190 to over 1,600 Gm, and toxic symptoms appeared as early as 42 days and as late as 22 months after the start of treatment

Five of the patients mentioned blurred vision as the most prominent visual symptom, one's initial complaint was blindness Four had peripheral neuritis only in the lower extremities Symptoms of spinal cord damage, motor involvement, or neuritis of the upper extremities or face were not described Only one patient had permanent impairment of vision (case 3) The peripheral neuritis resolved in all except our patient who still had minor residual symptoms 13 months after onset Some form of vitamin therapy was used in all but cases 3 and 5

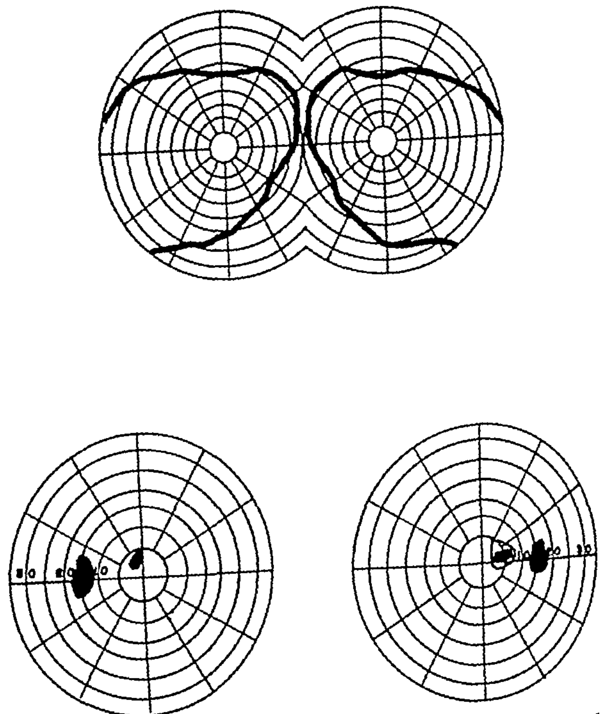

Fig 3 —Visual fields at examination on May 8, 1958, after resolution of all visual symptoms and retinal abnormalities Visual fields of April, 1959, are unchanged from these

The patient in case 3 had permanent visual impairment and the one in case 5 did not There are well-known neurotoxic symptoms associated with chemotherapeutic agents, such as streptomycin,[4] sulfa drugs,[13] cycloserine,[4] and isoniazid[14] Only our patient received a sulfonamide, and only the patients in cases 4 and 5 received streptomycin

The reasons for the neurotoxicity of chloramphenicol are not known Allergic or idiosyncratic mechanisms have been postulated for the hematopoietic toxicity[2] An allergic etiology cannot be eliminated, and it is worth noting that the patient in case 5 and our patient had intermittent exposures to the drug The findings are not unlike those of a vitamin deficiency,[15] and chloramphenicol does have marked effects on gastrointestinal tract bacteria[4] This suggests, but does not establish, the possibility of interference with normal vitamin metabolism The prompt response to vitamin therapy may support this concept, but in all cases the use of the drug was also discontinued It may be that chloramphenicol interferes at the cellular level and is similar to the effect of isoniazid on pyridoxine metabolism[16]

Neurological toxicity was not seen in one series of 1,510 patients given chloramphenicol, and the authors stated that they had concurrently given 'massive doses of vitamins B and C during therapy"[1] Perhaps some consideration should be given to the use of concurrent prophylactic doses of vitamins in patients who must receive chloramphenicol for long periods of time

Review of Cases of Optic and Peripheral Neuritis in Patients Receiving Chloramphenicol Therapy

Case No and Reference	Disease Treated*	Age Yr & Sex	Time of Administration Before		Chloramphenicol Toxicity						
			Total Dose Gm	Onset of Symptoms Days	Visual Symptoms	Visual Findings	Peripheral Neuritis	Other Toxic Symptoms	Therapy of Toxicity	Other Drugs	Response
1 Cewin and Friou[17]	SBE due to Staph aureus	29 M	190 5	66	Yellow vision blurred reading	Blurred disks enlarged blind spots granular changes in retinal pigment layer	Numbness tingling in both feet	Nausea vomiting hepatitis rash oral lesions	Vitamins A C D B complex and B_{12}	Chlortetracycline	Vision normal in 39 days neuritis lasted 14 days longer
2 Wallenstein L and Snyder J Ann Int Med 36 1526 1952	Ulcerative colitis buttocks abscess	24 F	427 5	171	Blurred vision	Acuity to 20/200 relative central scotomas blurred optic disks	Numbness tingling in both feet	Granulocytopenia	Vitamin B complex	Vitamin tablets (type not specified)	Vision normal in 39 days neuritis lasted 57 more days
3 Jasky M A and others J A M A 151 1403 1953	SBE due to Staph aureus	14 M	252 0	42	Blindness	Blurred disks acute retinal hemorrhages	None	Anemia acne mild urticaria	None	None	123 days later OS 20/200 scotoma constricted peripherally OD finger visible at 2 ft
4 Cole J G and others Am J Ophth 44 18 1957	SBE	44 M	323 0	199	Blurred vision therapy continued for 21 days after onset	Edematous disk constricted visual field	Numb feet	None	Thiamine vitamin B_1 acetazolamide (Diamox)	Penicillin Streptomycin (not given concurrently with chloramphenicol)	Vision normal in 30 days
5 Prevatt and Hunt[3]	Chronic melioidosis	32 M	>1 600 0†	22 mo	Smoky vision (3 repeat episodes)	Disks normal visual fields normal	None	Tinnitus	None	ACTH streptomycin chlortetracycline tetracycline	Abrupt relief when administration of drug was stopped
6 Present case	Chronic melioidosis	20 M	122 0	144	Blurred vision inability to focus	Papilledema constricted visual fields	Numbness in toes burning in feet	Neutropenia	Vitamins B complex B_{12} C and pyridoxine	Novobiocin sulfisoxazole (Gantrisin)	Vision normal in 63 days neuritis diminished but still present 13 mo later

* SBE = subacute bacterial endocarditis
† Intermittent administration

We do not recommend decreasing the use of chloramphenicol, nor do we suggest the production of a "polypharmacy pill combining chloramphenicol with vitamins We do believe, however, that neurotoxicity due to chloramphenicol is more frequent than is commonly recognized,[17] and we suggest that careful neurological and ophthalmologic examinations be made before and during the use of this drug If symptoms of decreased visual acuity or peripheral neuritis occur during the course of therapy with chloramphenicol, the prompt withdrawal of the drug and the institution of therapy with large doses of vitamins of the B group may prevent serious complications

Summary

Chloramphenicol given in large doses or for long periods appears to have a neurotoxic effect, particularly on the optic nerve If this is unrecognized or untreated, permanent blindness may result Large doses of vitamins, especially of the B group, and prompt withdrawal of the antibiotic may prevent these complications Frequent questioning and examination of the patient receiving chloramphenicol is recommended in order to detect toxicity

Lieut Col Frank L Miller and Capt Frederick S Davis helped in the management of this case

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GOUT, MYXEDEMA, AND HYPEROSTOSIS FRONTALIS INTERNA

REPORT OF CASE IN NEGRO WOMAN

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and
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Gout in a Negro woman is rare, there are only four reports in the literature [1] Hyperostosis frontalis interna (Morgagni-Stewart-Morel syndrome) [2] is not uncommon and is associated with obesity, hypertension, and nervous, metabolic, and endocrine disturbances Myxedema,[3] as well as gout,[1] has been previously reported in association with hyperostosis frontalis interna However, the unique combination of gout, myxedema, and the classical features of hyperostosis frontalis interna in a Negro woman has never been recorded

A 66-year-old Negro woman was admitted to the Maricopa County General Hospital with complaints of pains in her knees, ankles, hips, and the great toes of both feet of eight years' duration In addition, she complained of puffiness of both eyelids, swelling of the face, intolerance to cold, and dryness of the skin Her hair became brittle and began to fall out She complained of frontal and occipital headaches, nervousness, constipation, fainting spells, and irregular menses At about the age of 50 years, shortly after her initial complaints of pains in the joints, particularly about the great toes, her weight increased from 135 to 228 lb (61 to 103 kg) An initial attack of arthritis and redness, swelling, and excruciating pain over the metatarsal phalangeal joints of both great toes occurred in 1951

Onset of her menses occurred when she was 11 years old, and her periods were irregular She had had two miscarriages and one full-term pregnancy Menopause occurred at the age of 44 years A fluctuating type of hypertension was noted throughout the previous 10 years, with a range in blood pressure from 200/102 to 170/80 mm Hg There was no family history of gout, thyroid disease, tuberculosis, diabetes, or cancer, however, she stated that obesity was common in her family

Physical examination revealed a well-nourished Negro woman who appeared chronically ill Examination of the head revealed a sparseness of hair over the scalp Her facies were characterized by puffy eyelids and a dull, disinterested expression Her skin was dry The subcutaneous tissue was doughy There was a bilateral hallux valgus There

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From the Department of Medicine Maricopa County General Hospital was pain and tenderness over both knees and ankles, and there was marked swelling, tenderness, and pain on motion of the metatarsal phalangeal joints of both great toes The joints were warm and slightly red in appearance, and the skin was shiny The ankles were edematous

A hemogram showed normal findings, urinalysis gave normal results, as did serologic test for syphilis An x-ray of the chest revealed cardiac enlargement, the lung fields were normal Degenerative osteoarthritis of the dorsal spine was noted A series of tests on the upper gastrointestinal tract revealed a duodenal diverticulum An intravenous pyelogram showed normal findings The electrocardiogram showed nonspecific myocardial changes The blood urea nitrogen level was 7 5 mg per 100 cc Results of serum protein-bound iodine determinations were 1 8 and 2 1 mcg per 100 cc Serum uric acid levels were as follows 10 0, 10 3, 13 0, 13 4, 10 7, and 13 2 mm % The basal metabolic rate was —42% The serum cholesterol level was 245 mg % The urinary 17-ketosteroid and 17-hydroxy-corticoid levels were within normal limits Roentgenogram of the skull revealed marked hyperostosis frontalis interna (see figure) A roentgenogram of both feet showed an irregularity in the contour of the juxta-articular portions of the first metatarsal phalangeal joints of both great toes The left foot revealed punched-out areas compatible with the diagnosis of gouty arthritis Aspiration of both swollen areas over the great toes yielded a chalky white fluid which was identified as sodium urate crystals

Her clinical course in the hospital was as follows She was treated with colchicine, and dramatic relief of pain and swelling of all the joints occurred She was then placed on therapy with probenecid and good control of her symptoms of gouty arthritis was obtained The puffy eyelids, facial edema, and muscular aches were dramatically relieved by administration of whole desiccated thyroid, which also produced a general sense of well being

Comment

Gout is rarely seen in women, about 95% of all cases occur in men ⁵ It occurs infrequently in Negroes This patient s history of an attack in a great toe, persistent hyperuricemia, subcutaneous and osseous tophi, identification of uric acid crystals, roentgenographic evidence of gouty arthritis, and the dramatic clinical response to colchicine therapy fulfill the criteria for the diagnosis of gout

Thickening of the internal table of the frontal bone occurs in association with obesity, hypertension, and psychiatric, endocrine, and metabolic disturbances This condition, which at first was considered a rarity, occurs more frequently than is commonly supposed Hyperostosis frontalis interna has protean manifestations, of which the hyperostosis, although the most certain objective roentgenographically visible sign, may in effect be the least important[6]

The etiology of this syndrome is unknown Dyspituitarism has been considered an etiological factor because of the frequent association of hypertension, hirsutism, amenorrhea, sterility, and obesity which, at times, resemble Cushing's syndrome However, this has not been confirmed by autopsy and endocrine studies The hypothalamus may be the seat of the disturbance The occurrence of metabolic and endocrine disturbances in this syndrome is more common than could be explained on a coincidental basis Many patients have diabetes mellitus or exhibit a diminished glucose tolerance The coexistence of gout and hyperostosis was observed by Feiring[4] Harding[3] reported one case of myxedema and two cases of probable hypothyroidism in a series of 17 patients who had hyperostosis frontalis interna Since the condition is frequently familial and accompanied by other metabolic disorders, we believe it is probably among the inborn errors of metabolism

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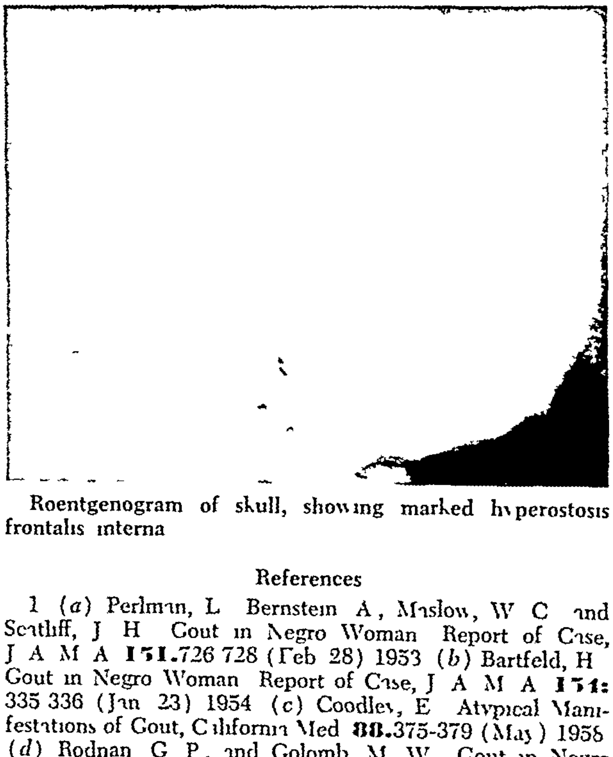

Roentgenogram of skull, showing marked hyperostosis frontalis interna

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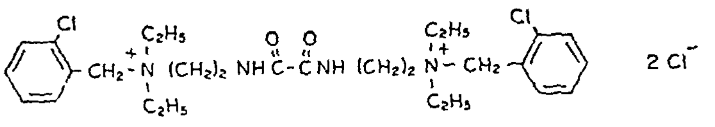
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council

H D Kautz, M D, *Secretary*

Ambenonium Chloride (Mytelase Chloride)—N,N′-Bis-2 [(2-chlorobenzyl) diethylammonium chloride]-ethyloxamide —N,N′-Bis (2-diethylaminoethyl) oxamide bis-2-chlorobenzyl chloride —The structural formula of ambenonium chloride may be represented as follows



Actions and Uses—Ambenonium chloride, a cholinesterase inhibitor having actions similar to those of neostigmine is used in the management of myasthenia gravis, in which it effects a substantial increase in muscular strength It, thereby, alleviates the principal manifestations of the disease generalized weakness and fatigability, ptosis, diplopia, blurred vision, difficulty in swallowing and articulating, and, in severe cases, respiratory embarrassment The therapeutic response to the drug is comparable to that to neostigmine and other cholinomimetic compounds, which, as a group, are the most effective of the available antimyasthenic agents Like other drugs of this group, however, ambenonium chloride produces only transient symptomatic improvement and is in no sense curative In severe myasthenia, it is usually impossible, even with optimal dosage, to completely restore the patient's muscular strength to normal Patients whose symptoms have become refractory to neostigmine or other older drugs are not likely to respond to ambenonium chloride, although the latter may be tried on an empirical basis Ambenonium is often useful in patients who cannot tolerate neostigmine because of individual idiosyncrasy

Two advantages have been ascribed to ambenonium chloride in comparison with neostigmine 1 Most, but not all, clinicians feel that the newer drug has a somewhat more sustained effect, permitting less frequent dosage and making possible a more uniform maintenance of muscular strength 2 Ambenonium is said to have a lower incidence of side-effects, especially gastrointestinal reactions Although this relatively late appearance of minor untoward effects, as dosage is increased, is generally acknowledged, it is regarded by some clinicians as disadvantageous since little warning is given of the imminence of serious overdosage

Side-effects, largely cholinomimetic and usually indicative of overdosage, include excessive salivation and sweating, nausea, vomiting, abdominal cramps, diarrhea, miosis, and urinary urgency These effects can be minimized by precise adjustment of dosage Routine administration of atropine to combat them is unwise, since they serve as useful signals of incipient toxicity and a warning of the imminence of more serious nicotinic effects of overdosage such as muscular fasciculation, weakness, and paralysis, which are not controlled by atropine However, even when anticholinergic agents are not administered, gastrointestinal symptoms associated with ambenonium therapy may not appear until late In this case, muscular weakness may be the earliest sign of overdosage An occasionally reported reaction that is not seen with the administration of neostigmine is characterized by jitteriness, dizziness, headache, and mental confusion

Ambenonium chloride exerts its effects by reversibly inactivating cholinesterases and, thereby, potentiating the effects of endogenous acetylcholine In addition, there is suggestive evidence that the drug also may stimulate the motor end-plate through another mechanism as yet poorly elucidated In experimental nerve-muscle preparations, low concentrations increase the response of skeletal muscle to indirect stimulation and antagonize the effects of tubocurarine, higher concentrations produce neuromuscular blockade and paralysis Ambenonium chloride is relatively more selective in its inhibition of acetylcholinesterase, as opposed to nonspecific cholinesterases, than is neostigmine Like other quaternary ammonium compounds, it penetrates the blood-brain barrier only poorly

Dosage—Ambenonium chloride is administered orally As with other drugs used in the management of myasthenia gravis, the dose of ambenonium chloride should be carefully adjusted for each patient in accordance with response and tolerance The suggested initial dose is 5 mg, dosage is then gradually increased as required When the disease is of moderate severity, 5 to 25 mg three or four times daily constitutes an average dose It must be remembered that the dosage requirement varies considerably with spontaneous fluctuations in the severity of the disease and may be increased in the postpartum period and by intercurrent infection, emotional disturbances, and by other factors When the total daily dosage exceeds 200 mg, the likelihood of serious toxic effects necessitates unusually careful observation of the patient by the physician

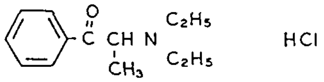
When muscular weakness becomes more severe during therapy with ambenonium chloride, it must be determined whether this complication is caused by an exacerbation of the disease or by overdosage of the drug When excessive dosage is at fault, other cholinomimetic symptoms are almost always present Should signs of overdosage appear, administration of the drug is discontinued and 0 5 to 1 mg of atropine sulfate is given slowly by intravenous injection Artificial respiration, administration of oxygen, and other supportive measures are instituted as needed

Ambenonium chloride should be used with great caution in the presence of bronchial asthma and intestinal or urinary tract obstruction

Preparations —tablets 10, 25 mg

Year of introduction 1958
Winthrop Laboratories, Division of Sterling Drugs Inc , cooperated by furnishing scientific data to aid in the evaluation of ambenonium chloride

Diethylpropion Hydrochloride (Tenuate, Tepanil) —2-Diethylaminopropiophenone hydrochloride —1-Phenyl-2-diethylaminopropanone-1 hydrochloride —The structural formula of diethylpropion hydrochloride may be represented as follows



Actions and Uses —Diethylpropion hydrochloride, a sympathomimetic amine chemically related to amphetamine, is used clinically for the purpose of suppressing appetite and thereby reducing food intake in the management of obesity It has not been conclusively shown to differ significantly in its use for this purpose or in its actions and side-effects from other amphetamine-like compounds Thus, the chief effect of the drug is to lessen by virtue of its anorexigenic action the distress attendant on strict adherence to a diet, especially during the early phases of dieting There is little evidence, however, that prolonged usage continues to promote loss of weight indefinitely during long-term therapy, nor is there reason to believe that reduction of appetite persists after administration of the drug is stopped Hence, reeducation of the patient with respect to eating habits and removal of underlying psychological and physical causes of overeating remain the only effective means of bringing about and maintaining loss of weight over a long-term period

The claim that diethylpropion hydrochloride, in effective anorexigenic doses, produces fewer side-effects than do similar drugs lacks conclusive substantiation However, symptoms attributable to central nervous system stimulation, such as anxiety, jitteriness, and insomnia, have not been stressed in the few clinical reports that have been made Cardiovascular stimulation, including palpitation, tachycardia, and elevation of blood pressure, also seems to have been minimal

The possible adverse effects of the drug when it is administered over long periods of time have not been thoroughly investigated Although chronic toxicity studies have disclosed no deleterious effects on the liver, kidney, or blood-forming tissues, the reported studies are considered inadequate Little is known about the acute pharmacodynamic properties of the compound

Since diethylpropion hydrochloride has not been shown to be more effective than other amphetamine-like agents and since its possible toxic effects have been less thoroughly explored than have those of some older drugs, there would seem to be little reason for its choice in preference to established anorexigenic agents, unless the suggested lower incidence of side-effects can be conclusively established

Dosage —Diethylpropion hydrochloride is administered orally The usual dose is 25 mg three or four times daily

Preparations —tablets 25 mg

Year of introduction 1959
The Wm S Merrell Company and the National Drug Company cooperated by furnishing scientific data to aid in the evaluation of diethylpropion hydrochloride

APOTHECARY'S FEES

Charges for drugs, parenthetically, at times bulked larger than fees in medical bills—the usual situation in an apothecary's practice The busy Dr Hugh Mercer of Fredericksburg, for example, was charging, by the early seventies, 5 shillings for a visit but no less than 7/6 for doses of galap—the latter figure being about the price of two pairs of shoes No wonder that when one Dr James McClurg rejected the functions of both surgeon and apothecary, he could not make a living, and that simply as abstention from drug selling aroused professional resentment against Dr Adam Thompson at Philadelphia in 1748 — Shryock, R H , Medicine and Society in America, 1660-1860, New York University Press, 1960, pp 12-13

ORGANIZATION SECTION

STATEMENT BEFORE THE SENATE FINANCE COMMITTEE ON H R 12580, 86TH CONGRESS

By Leonard Larson, M D June 30, 1960

Mr Chairman and Members of the Committee

I am Dr Leonard Larson of Bismarck, N D I am appearing here today as the President-elect of the American Medical Association With me is C Joseph Stetler, Director of the Legal and Socio-Economic Division of the Association

With your permission, Mr Chairman, we should like to file for the record a full statement of our views on Title VI of H R 12580 Because the Committee's time is limited, my oral testimony will deal very briefly with the matters discussed in this document

The American Medical Association urges passage of Title VI for three main reasons

1 It is designed to help those who really need help It does not make the mistake of treating our 15½ million older people as a homogeneous group requiring an across-the-board approach By providing aid only to those who need aid, it preserves the right of the non-needy to take care of themselves

2 Title VI, by limiting its effect to the near-needy minority, allows the majority to continue its use of the voluntary method The measure is in no sense compulsory

3 Title VI makes the states primarily responsible for administration of the program—not the federal government We are convinced that the health care costs of the needy and near-needy can best be determined and met locally

Any legislative proposal which seeks to meet the problems confronting the aged should be considered with these things in mind

—The economic status of the aged is a great deal better than it is customarily pictured to be, with the vast majority of our 15½ million people over 65 capable of meeting the costs of health care without undue difficulty

—Contrary to popular misconception, the majority of our aged are in good health—neither sick nor debilitated

The needs of those who are sick or disabled are being met primarily through private resources, health insurance and prepayment plans, and the voluntary efforts of their families and private citizens working together at the community level

We should therefore concern ourselves not with the majority, which is neither disabled nor destitute, but with the minority

There are, of course, many persons over 65 who have serious problems Two and one-half million are now on Old Age Assistance, and an undetermined additional number, although able to finance other costs of living, find it almost impossible to withstand the additional burden of the cost of illness Even here, however, the picture is not discouraging In 1950, 22% of all persons over 65 received Old Age Assistance In 1959, it was reduced to 15%, and government figures indicate that this percentage should drop to 11% by 1970 Thus, the improving economic status of the aged is reflected in a continuing reduction in the number of persons who receive Old Age Assistance

It is the needy and near-needy which Title VI would help effectively

The American Medical Association emphatically favors helping those who need help But the Association does not believe this necessitates the creation of massive federal machinery to help those who neither need nor want help, and who are capably handling their own problems at the present time

This brings us to the question of who should provide whatever help is needed

At the Annual Meeting in June of the American Medical Association, the following statement was adopted by our House of Delegates as the policy of the A M A I should like to read it to you

"Personal medical care is primarily the responsibility of the individual When he is unable to provide this care for himself, the responsibility should properly pass to his family, the community, the county, the state, and only when all these fail, to the federal government, and, then, only in conjunction with the other levels of government, in the above order The determination of medical need should be made by a physician, and the determination of eligibility should be made at the local level with local administration and control The principle of freedom of choice should be preserved The use of tax funds under the above conditions to pay for such care, whether through the purchase of health insurance or by direct payment, provided local option is assured, is inherent in this concept"

It is clear that the policy of the American Medical Association is in no way incompatible with the principles upon which Title VI is based

Regrettably, the financing of medical care for the aged has produced violent controversy both in and out of Congress There are two schools of thought as to how it should be handled

On the one hand are the proponents of Old Age and Survivors Disability Insurance (OASDI) health care amendments, who propose that a radical change be made in what is essentially a cash benefit program Disregarding the fact that such a course can lead only to state medicine, the advocates of this approach call for federal intervention via compulsory Social Security taxation for the financing of medical benefits for all OASDI beneficiaries—regardless of need

Such a program would compel the non-needy to accept federal medicine rather than buy medical care voluntarily through their own resources In fact, the proponents of this plan oppose the right of individuals to pay voluntarily for their own health care, for they insist that the federal government assume this responsibility for everyone eventually—beginning with the aged

This is the outright socialization of the financing of medical care, and we are strongly opposed to it for reasons which we have detailed at some length in the written attached statement

To mention just a few of those reasons briefly, such a program would be unpredictably costly, it would unnecessarily cover millions of people, it would substitute service benefits for cash benefits, it would lead to a poorer—not better—quality of medical care, it would overcrowd our hospitals, it would lead to the decline, if not the demise, of private health insurance, and it would interfere dangerously with the doctor-patient relationship which is the solid foundation upon which effective medical care must be based

In contrast to the OASDI approach is the federal grant-in-aid program for the medical care of the near-needy, to be administered locally for locally determined beneficiaries whose eligibility is also determined at the local level This is the method adopted by the House of Representatives by an overwhelming majority It is a method which preserves "voluntaryism", which permits the non-needy to take care of themselves This follows the traditional federal-state organizational structure of our nation

It is the economical method, which maintains local autonomy

It is, therefore, the antithesis of the centralized, socialized, statist approach of the Forand-type proposals

While helping those who need help, it preserves the right of self-reliant individuals to finance their own health care, and bases its approach to the problem on family and community responsibility

This program has been criticized as modest —presumably because its effect would be confined to the needy and near-needy, instead of to millions of older people who neither want nor need federal government help

To those critics who call this program modest, we say that fiscal irresponsibility, unpredictable cost, and maximum nationalization are not the accepted criteria for good or adequate legislation

We believe that Title VI merits the support of everyone familiar with the problem

We believe that the House Ways and Means Committee is to be commended for its wisdom and statesmanship in developing so sound a proposal

We urge this Committee to accept the carefully considered conclusions of the House, based, as they have been, on months of intensive study

In closing, let me repeat that we physicians believe in helping those who need help We have bent our efforts toward providing this help for as long as our profession has existed We are resolute in our determination to continue in this course

DR KAUTZ LEAVES COUNCIL ON DRUGS

Dr Harold D Kautz, Secretary of the Council on Drugs, resigned from the staff of the A M A to accept a position as Director of the Division of Product Information in the Medical Department of Abbott Laboratories, North Chicago, Ill He had served for 21 years as a member of the Council staff Dr Christian Wingard has been promoted from Assistant Secretary to Associate Secretary of the Council and will assume full responsibility for the operation of the Council's drug evaluation program He will also endeavor to carry on the activities of the Council, pending the appointment of a new secretary Another Assistant Secretary, Dr John R Lewis, joined the Council staff on July 1 to assist Dr Wingard in the operation of the drug evaluation program

Dr Kautz came to the A M A Council in June, 1939, when it was known as the Council on Pharmacy and Chemistry He was the sixth secretary since the Council, second oldest in the A M A organization, was organized in 1905 as a standing committee of the Board of Trustees Dr Kautz received his M D degree from the University of Nebraska College of Medicine, Omaha, in 1937

AWARD FOR FILM ON HOSPITAL SEPSIS

The motion picture entitled "Hospital Sepsis a Communicable Disease" was given the Blue Ribbon Award by the American Film Festival as the best medical film produced in the past year It was chosen from a selected group of medical films which were exhibited at the American Film Festival in New York This film was sponsored by the American Medical Association in cooperation with the American College of Surgeons and the American Hospital Association with a grant from Johnson and Johnson It was produced by Churchill Wexler Studios in Hollywood More than 500 copies of this film have been distributed on a world-wide basis and narrated in English, Spanish, Portuguese, and German

MEDICAL NEWS

CALIFORNIA

Hospital to Manage Artery Bank—Management of what is reported to be the nation's first licensed artery bank has been accepted by the Hospital of the Good Samaritan, Dr Arthur Fernfield, president of the Los Angeles County Heart Association, announced July 21 The Artery Bank, established in 1954 and serving the Southwest, has been directed by the heart association's Artery Bank Committee, headed by Dr L John Tragerman, chief pathologist of the Good Samaritan Hospital Approval of the State Board of Public Health was recently given Dr Tragerman will represent the hospital on the heart association's Community Services Committee and will continue to be in charge of the Artery Bank

Society News—The new officers of the Los Angeles Pediatric Society for 1960-1961 are Drs Lawrence S Siegel, president, Neil N Litman, vice-president, and Leslie M Holve, secretary-treasurer ——At the annual banquet of the Beverly Hills Academy of Medicine the following officers were installed for 1960-1961 Drs Seymour L Cole, Los Angeles, president, Harold C Fishman, vice-president, and Bernard G Sarnat, secretary-treasurer The annual prize for the best paper published by a member during the previous year was awarded to Dr Julius H Winer The title of the paper was "Practical Value of Analysis of Urinary Calculi"

Hospital Conference on Genetics and Mental Disease—The second invitational conference, "Metabolic Errors, Genetics, and Mental Disease," of the Napa State Hospital, Imola, presented by Napa and Sonoma State hospitals in cooperation with the Ames Company, Inc, will be held Oct 8 The meeting will be limited to 120 professional persons, including psychiatrists, psychologists, biochemists, geneticists, pediatricians, and other interested persons Participants will include Dr David Yi-Yung Hsia, Chicago, Norman E Kretchmer, Ph D, Stanford, Dr Stanley W Wright, Los Angeles, Dr Willard R Centerwall, Los Angeles, Dr Alfred G Knudson, Jr, Los Angeles, Jon Karlsjon, Eldridge, Dr Carolyn W F Piel, San Francisco, and Dr Robert W Day, Eldridge For information, write Dr David W Wardell, Chief of Professional Education, Sonoma State Hospital, Eldridge, Calif

COLORADO

New Quarters for Health Department—The Colorado State Department of Public Health, including the laboratory and all divisions and sections, is now located in the new State Health Department Building at 4210 E 11th Ave, Denver 20 (Phone DUdley 8-5801) Dr Roy L Cleere is executive director

INDIANA

Surgeons to Hold Annual Regents Meeting—The Indiana Division of the United States Section, International College of Surgeons, will hold its annual regents meeting at the Indiana University Medical Center, Indianapolis, Sept 14 Dean John D Van Nuys of the Indiana University Medical Center will open the program with an address The following papers are scheduled

Acute Renal Failure, Dr Hunter A Soper, Indianapolis
Current Virus Research, Dr Clyde G Culbertson, Indianapolis
Abdominal Bruits and Echymoses of Diagnostic Significance, Dr Alfred D Dennison Jr, Indianapolis
Clinical Application of Cineradiography, Dr John A Campbell, Indianapolis
Management of Varicose Veins, Dr Earl O Latimer, Chicago
Anatomical Factors of Importance in Surgery of the Biliary Passages, Dr Manuel E Lichtenstein, Chicago
Hazards of Modern Diagnosis and Treatment, Dr Edward B Smith, Indianapolis
Treatment of Pneumothorax, Dr Joseph C Finneran, Indianapolis

An evening banquet is planned All surgeons and medical practitioners are invited For information, write Dr Simon Reisler, 318 Bankers Trust Bldg, Indianapolis 4

IOWA

Ophthalmology and Otolaryngology Meeting—The Iowa Academy of Ophthalmology and Otolaryngology will hold its annual meeting Sept 14-16, at the New Inn, Okoboji Speakers and topics for the scientific program are as follows Dr Robert H Foss, Des Moines, "A Story of Service to Ophthalmology and the American People", Mrs Ruby Hopkins, New York City, "New Activities of the National Society for Prevention of Blindness", Dr Chester C Woodburn Jr, Des Moines, "Management of Fractures of the Jaw", Dr John E Harris, Minneapolis, "The Cornea Basic and Clinical Considerations", and Dr Jerome A Hilger, St Paul, "The Surgical Repair of Facial Injuries" and "The Surgery of Hearing Loss" Officers for the coming year will be elected, and a banquet, sports events, and dance are planned

KANSAS

University of Kansas Awarded Cancer Research Grant—The University of Kansas Medical Center in Kansas City has been given a $400,000 contract by the U S Public Health Service to study agents that may identify viruses causing human cancer

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health Programs should be received at least three weeks before the date of meeting

The Kansas group, one of 100 such research teams working on the National Cancer Institute's virology programs, will be headed by Dr Herbert A Wenner

LOUISIANA

Tulane Appoints New Anatomy Chief—James A Miller Jr, Ph D, has been appointed professor and chairman of the department of anatomy at Tulane University of Louisiana School of Medicine, New Orleans He assumes the post formerly held by Dr Harold Cummins, who retired a year ago and is now assistant dean of admissions Dr Miller received his Ph D degree in zoology from the University of Chicago and has served on the faculties of Ohio University, University of Michigan, and University of Tennessee He has taught at Emory University since 1946 In 1959 Dr and Mrs Miller received the annual Research Citation of the Emory chapter of Sigma Xi in recognition of their research on asphyxia of the newborn

Dr Caldwell Retires as Clinic Director—The Ochsner Clinic, New Orleans, announced May 1 the appointment of Dr Merrill O Hines as medical director for the clinic and the retirement of Dr Guy A Caldwell from the position Dr Caldwell, a founding partner of the clinic and its medical director since 1954, will continue to serve as a trustee and vice-president of the Alton Ochsner Medical Foundation In addition, he will act as a consultant to the clinic's department of orthopedic surgery, which he headed from 1942 until his retirement from active medical practice in 1957 Dr Hines, head of Ochsner Clinic's department of proctology since 1946 and assistant medical director since 1954, is president-elect of the American Proctological Society He is a member of the American Board of Proctology and the Residency Review Committee of the A M A

MARYLAND

Maryland Academy to Hold Assembly—The 12th annual scientific assembly of the Maryland Academy of General Practice will be held at the Southern Hotel, Baltimore, Oct 8-9 Included in the topics to be discussed are penicillin, 'CVA" diagnosis, chronic arthritis, contact dermatitis, immunology, anticoagulant therapy, diabetes, and office gynecology and cancer protection A banquet, business meeting, and entertainment are planned For information, write Dr C P Crimy, Secretary, 2722 E Monument St, Baltimore 5

MASSACHUSETTS

Establish Degree of Doctor of Nursing Science—A doctor of nursing science degree, the first doctorate in the country which specifically identifies nursing in the degree title, has been established at the Boston University School of Nursing, according to the school's Dean Marie Farrell, of Newton The first doctoral offering is in psychiatric nursing, with programs in other clinical areas to be instituted in the next two to four years Previously, the highest level of training offered at the school was the Certificate of Advance Professional Specialization, consisting of a minimum of 30 semester hours of advanced study beyond the master's degree The new degree program calls for a minimum of 60 semester hours' credit in advanced, directed study, plus a doctoral dissertation

Appoint Head for Biological Chemistry Departments—Eugene P Kennedy, Ph D, has been named Hamilton Kuhn Professor of Biological Chemistry and head of the department of biological chemistry at the Harvard Medical School, Boston His appointment is effective Sept 1 Currently Dr Kennedy, who is professor of biological chemistry at the University of Chicago, is on leave while serving as a senior postdoctoral fellow of the National Science Foundation at Oxford University, England The Hamilton Kuhn Professorship of Biological Chemistry was founded in 1909 under the will of Mrs Hartman Kuhn in memory of her son Dr Kennedy has been a member of the faculty at the University of Chicago since 1951 In recognition of his contributions to biological chemistry, he received the Glycerine Research Award in 1955 and the Paul–Lewis Award of the American Chemical Society in 1958

Personal—On July 20, delegates to the fourth conference of the Industrial Council for Tropical Health paid tribute to a co-founder of the conference, Dr George M Saunders, medical director of the Socony Mobil Oil Company, Inc Dr Saunders was presented with a citation containing 'the acknowledgment of his colleagues in industrial and academic medicine in grateful recognition of his distinguished contributions to international health'——Dr Howard H Hiatt, a research scientist at Beth Israel Hospital and Harvard Medical School, will leave Boston in August to spend one year at the Pasteur Institute in Paris, France, on a traveling fellowship awarded to him by the Commonwealth Fund——Dr Herrman L Blumgart, professor of medicine, Harvard Medical School, has been reappointed for a five-year term as editor-in-chief of *Circulation*, monthly professional journal of the American Heart Association

MICHIGAN

Report Decline in Birth Rate—According to provisional figures released July 21 by the Michigan Department of Health, there were 1,405 fewer births in Michigan during the first three months of 1960 than last year during the same period There were 42,463 babies born in the first quarter compared with 43,868 in 1959 If the trend continues, 1960 will be the third straight year of decline since 1957, when 208,488 births were recorded In 1958 there were 202,690 births and this was the first year since 1948 that births had not increased in Michigan In 1959, only 197,809 births were recorded, according to the state health department

Society News—The Michigan Allergy Society announced the election of the following officers for the year 1960-1961 Drs Robert G Lovell, Ann Arbor, president, Alex S Friedlaender, Detroit, vice-president, Hilda M E Hensel, Monroe, secretary, and Israel Wiener, Detroit, treasurer ——At the annual meeting of the Academy of Surgery of Detroit May 12, Dr Edward K Isbey, Center Line, accepted the presidency from outgoing Dr Joseph A Witter, Highland Park New officers elected *were president-elect, Dr Clifford D Benson*, Detroit, and secretary-treasurer, Dr Donald N Sweeny, Detroit The Angus McLean Award was presented to Dr Angelos A Kambouris, Detroit, for his prize-winning paper

MINNESOTA

Dr Bowen Leaves for Africa—Dr Ralph Bowen Jr, fellow in plastic surgery, Mayo Clinic, Rochester, has left for Nairobi, Kenya, East Africa He will spend a year in Africa, working under the sponsorship of the African Research Foundation and MEDICO At present, the heavily populated Nairobi area, where cancer of the skin is particularly prevalent, has only one plastic surgeon, Dr A Michael Wood, of Nairobi, executive director of A R F, with whom Dr Bowen will work Dr Bowen will carry on cancer research and will also be the only physician attached to a newly created mobile medical unit

NEBRASKA

Dr Levine Honored—Dr Victor E Levine, professor emeritus of biological chemistry, Creighton University School of Medicine, Omaha, will have his portrait added to the collection of the National Library of Medicine, Washington, D C This collection, including photographs and prints of "outstanding medical men" of the past four centuries, is being enlarged by addition of contemporaries "who have made significant contributions to the medical sciences" The National Library of Medicine was formerly known as the Armed Forces Medical Library

NEVADA

Surgical Meeting in Reno—The 10th annual conference of the Reno Surgical Society will be held at the Mapes Hotel, Reno, Aug 18-20 Fifteen papers are scheduled for presentation by the following speakers Drs John J Bonica, Tacoma, Wash, John E Dunphy, Portland, Ore, John H Lawrence, Berkeley, Calif, Jonathan E Rhoads, Philadelphia, J Max Rukes, San Francisco, Paul C Samson, San Francisco, Grantley W Taylor, Boston, and John C Ullery, Columbus, Ohio The program is acceptable for category II credit by the American Academy of General Practice President of the society is Dr Lowell J Peterson A panel discussion at the Aug 19 luncheon and a round-table discussion the morning of Aug 20 will feature a guest speaker For information, write Dr Gilbert G Lenz, 505 Arlington Ave, Reno, Nev

NEW YORK

Dr Warner Named Geriatrics Director—The appointment of Dr George M Warner as director of the State Bureau of Chronic Disease and Geriatrics was announced by Dr Herman E Hilleboe, State Health Commission Dr Warner has served as home care executive and deputy chief, division of social medicine, Montefiore Hospital, Bronx, since 1955 He succeeds Dr Frank W Reynolds, who resigned in September, 1959, to become associate professor of public health practice at the University of Michigan

Establish Physical Biology Department—Cornell University Medical College, Ithaca, on July 18 announced the establishment of a new department of physical biology to study the fate of radioactive metals in the body and their influence on normal body metabolism Cyril L Comar, Ph D, has been named head of the department Thirty-four professors and researchers at Cornell will make up the staff The new department will be part of Cornell's New York State Veterinary College Special emphasis in the department's work will be on the disease problems associated with radioactive fallout The new department grew out of the Laboratory of Radiation Biology which Professor Comar developed and which was part of the department of physiology in the Veterinary College Part of the department's work will be carried on at the Veterinary College and part in a new building complex which is being built on the campus with funds from Cornell and the United States Public Health Service and Atomic Energy Commission Professor Comar represented the United States at the International Congress on the Peaceful Use of Atomic Energy held at Geneva in 1955 He is a member of various U S teams dealing with the World Health Organization and is a consultant to the Food and Agriculture Organization, Atomic Energy Commission, Public Health Service, Oak Ridge Institute of Nuclear Studies, Stanford Research Institute, and American Institute of Biological Sciences

New York City

Society News—At the May meeting of the Brooklyn Radiological Society the following members were elected to office president, Dr George A Manfredonia, vice-president, Dr Isadore Katz, and secretary-treasurer, Dr Joseph P Arcomano, 168 Clinton St, Brooklyn 1 The society meets monthly, October through May, on the first Thursday of each month ——The Brooklyn Psychiatric Society elected the following officers for the year 1960-1961 presi dent, Dr Abbott A Lippman, vice-president, Dr Edward F Falsey, and secretary, Dr Morton M Golden

Personal—On May 4, in a ceremony at the United Nations, Dr George T Pack was awarded the Order of Rubin Dario with the rank of Great Silver Cross, presented by Ambassador Guillermo Lang in behalf of President Luis Somoza of Nicaragua, in "recognition of services to the cancer program' of that country —Dr Benjamin H Kean, associate professor of clinical medicine (tropical medicine), Cornell University Medical College, is making a round-the-world trip on behalf of the Ford Foundation, which he serves as medical consultant Egypt, Ethiopia, Iran, Pakistan, India, Burma, Indonesia, and the Philippines will be visited in an effort to evaluate the medical attention available to Americans abroad

NORTH CAROLINA

First Moore Lecture Given—The first Julian A Moore Lecture was presented June 20 to members of the Buncombe County Medical Society by Dr Howard H Bradshaw, professor of surgery, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem The late Dr Moore was for many years a surgeon in Asheville Dr Bradshaw s address reviewed the development and progress in the surgical treatment of pulmonary tuberculosis Dr Theodore S Raiford, Asheville, society president, presided

OREGON

Dr Pickering Named Director of Primate Center—First director of the Oregon Primate Research Center, to be located near Portland, will be Dr Donald E Pickering, Doernbecher Professor of Pediatrics, University of Oregon Medical School, Portland, according to a joint announcement by officials of the Medical Research Foundation of Oregon and dean of the Medical School, Dr David W E Baird Jr Dr Pickering and Edward S West, Ph D, chairman of the biochemistry department, are principal investigators on the grants totaling $1,917,275 for construction of the center, which were made in April to the Medical Research Foundation by the U S Public Health Service Dr Pickering has conducted investigations with a colony of monkeys, which will serve as the nucleus of the larger number to be housed at the center

PENNSYLVANIA

Lay Editor to Receive Public Health Award—Dane S Wert, editor of the Harrisburg *Sunday Patriot-News*, has been selected to receive the 1960 lay individual Benjamin Rush Award of the Pennsylvania Medical Society as one 'who has made an outstanding voluntary contribution to the advancement of public health in Pennsylvania,' and the Pittsburgh Section of the National Council of Jewish Women will receive this year's lay organization award for having made a similar contribution voluntarily These awards will be presented at the annual session of the Pennsylvania Medical Society in Atlantic City in October A newspaperman for more than 15 years, Mr Wert recently established a science and medicine section in the *Sunday Patriot-News*

Personal—Drs Joe D Bentz and Thomas A Speer, Pittsburgh, were appointed as full-time plant physicians at Homestead District Works of United States Steel Corporation Dr Bentz was previously associated with the Pennsylvania Railroad and served for one year of in-plant training at the Westinghouse Atomic Energy Plant in Pittsburgh Dr Speer entered the U S Public Health Service in 1957, serving as medical consultant in civil defense to the State Health Department of Texas at Austin Later he was medical officer-in-charge of a U S P H S receiving center at El Centro, Calif —Dr Milton L McCall, chairman, department of obstetrics and gynecology, University of Pittsburgh School of Medicine, delivered the annual George Birney Broad Lecture at the State of New York Upstate Medical Center, Syracuse, April 19 Dr McCall spoke on Functional Gynecological Surgery"

Philadelphia

Alumni Election—New officers of the Temple University Medical Alumni Association are Drs Emanuel M Weinberger, president, David J Phillips, president-elect, Trudeau M Horrax, first vice-president, Fred Murtagh Jr, second vice-president, Walter J Levinsky, secretary, Fred B Rogers, corresponding secretary, and Paul R Casey, treasurer

Dr Beerman Honored by Dermatologists—In recognition of the long and devoted service' of Dr Herman Beerman to the Society for Investigative Dermatology, the board of directors of the society established an annual Herman Beerman Lectureship It is proposed that this lecture be given by a 'distinguished scholar at the annual scientific session of the society and that he be given an honorarium The incoming president of the society is to serve as chairman of the committee to select the speaker for the next annual meeting, and the board of directors is to serve as the committee

Personal—Dr John Kapp Clark on July 1 was named director of research and development at Smith Kline & French Laboratories Dr Clark, who had been SK&F s director of research, will continue his affiliation with the University of Pennsylvania, where he serves as associate professor of medicine —Marion Fay, Ph D, president and dean of Woman's Medical College of Pennsylvania, announced that Dr Irene E Maher, who has been assistant dean for 11 years, was given the title of associate dean at the June 24 meeting of the board of corporators, and that Dr Eva F Fox received the new appointment of assistant dean

Dr Ingalls to Head Phipps Institute—Dr Theodore H Ingalls, professor of preventive medicine and epidemiology at the University of Pennsylvania, has been made director of the university's Henry Phipps Institute He succeeds Dr Julius L Wilson, who has resigned to become director of medical education of the American Thoracic Society, New York City Dr Ingalls will maintain his classes in clinical epidemiology at the university's School of Medicine He will also continue to direct a study, supported by the Kellogg Foundation, for evaluation of periodic health examinations The Henry Phipps Institute, founded in 1903 for the study and treatment of tuberculosis, in recent years has broadened its research and teaching programs to include investigation of other chronic diseases

Reorganize Governing Board at Hahnemann—A major reorganization of the governing board of Hahnemann Medical College and Hospital was announced Newly created posts of chairman of the board and vice-chairman of the board of trustees were filled by former president Watson Malone III, president of Watson Malone and Sons, and former second vice-president, Carl S Vogel, vice-president of the Edgcomb Steel Company Elected as president of the corporation was Dr Charles S Cameron Jr, dean at Hahnemann Medical College for four years Vice-presidents elected were Robert Dunlop, president of the Sun Oil Company, and James M Britain Mr Charles S Paxson Jr, Hahnemann Hospital administrator was reelected as vice-president Dr Cameron will relinquish his duties as dean as soon as a replacement is appointed

Pennsylvanian Physicians Aid Moroccans—Five University of Pennsylvania doctors have volunteered to spend a month each as members of an international Red Cross team in Morocco treating 10,000 paralyzed victims of "adulterated cooking oil" Each doctor will act as delegate and medical advisor for the League of Red Cross Societies, which has been carrying on a rehabilitation program for the victims since they were stricken last fall The physicians will not be compensated for their professional services The American Red Cross will provide travel expenses, and MEDICO will provide funds for living expenses Those taking part in the project are Dr Wilmer M Anderson Jr, neurology instructor, Dr William J Erdman, director of the department of physical medicine and rehabilitation, Hospital of the University of Pennsylvania, Dr Albert A Martucci, associate professor of physical medicine and rehabilitation, Graduate School of Medicine, Dr David G Young, instructor in physical medicine and rehabilitation, Dr Igho H Kornblueh, director of physical medicine and rehabilitation, University of Pennsylvania Graduate Hospital At present, a medical staff of 50 from Red Cross societies in 13 nations are caring for the victims, most of whom are under 18 years of age

New Department Heads at Pennsylvania—Two appointments at the University of Pennsylvania School of Medicine have been announced Dr Harold G Scheie, professor of ophthalmology, has been named chairman of the department of ophthalmology, and Dr Harold S Ginsberg, of Western Reserve University School of Medicine, Cleveland, has been named professor and chairman of the department of microbiology Dr Scheie succeeds Dr Francis H Adler, emeritus professor of ophthalmology who served for 23 years as department chairman Dr Scheie received his M D degree from the University of Minnesota He served in 1959 as first vice-president of the American Academy of Ophthalmology and Otolaryngology and as Chairman of the Section on Ophthalmology of the A M A A brigadier general in the Army Reserve, he is a member of the Advisory Council on Reserve Affairs to the Surgeon General and of the Advisory Panel on Medical Sciences to the Secretary of Defense Dr Ginsberg has been associate professor of preventive medicine at Western Reserve since 1951 He received his M D degree at Tulane University School of Medicine, New Orleans His research activities include studies of basic aspects of virology at the Rockefeller Institute, the Yale School of Medicine, and Thorndike Memorial Laboratory in Boston City Hospital He is succeeding to the department chairmanship formerly held by Dr Stuart Mudd, emeritus professor of microbiology

VIRGINIA

Seminar on Kidney Disease—The Southeastern Region of the College of American Pathologists and the Virginia Society of Pathologists will hold a joint meeting at the John Marshall Hotel in Richmond Nov 25-26 on kidney disease The speakers will include Drs Stanley M Kurtz, Pittsburgh, Peter P Ladewig, Montgomery, W Va, Henry D McIntosh, Durham, N C, George Margolis, Durham, N C, Conrad L Pirani, Chicago, David E Smith, Charlottesville, and Maximilian Wachstein, Brooklyn The slide seminar will be conducted by Drs Paul Kimmelstiel, Charlotte, N C, and Solomon Papper, Boston The dinner speaker will be Dr Francis C Coleman, Des Moines, Iowa, president of the college The slide sets for this seminar on kidney disease may be purchased at a cost of $15 per set by writing to Dr Geoffrey T Mann, Professor of Forensic Pathology, P O Box 41, Medical College of Virginia, Richmond 19, Va

WEST VIRGINIA

Heart Association to Meet in Parkersburg—On Sept 16, the West Virginia Heart Association will hold its annual meeting at the Chancellor Hotel, Parkersburg The subject, Cardiac and Industry,' will be discussed by Dr A Carlton Ernstene, Cleveland, president, American Heart Association, Dr Herman K Hellerstein, Cleveland, Cleveland Clinic, Dr David Gelfand, assistant professor of cardiology, University of Pennsylvania, Philadelphia, Dr Eugene J Ryan, plant medical director, E I duPont de Nemours & Co , Belle, W Va , Dr R J Sexton, plant medical director, Union Carbide Chemicals Co , Institute, W Va , and Mr F Ray Power, director, State Vocational Rehabilitation Division, Charleston, W Va

Hospital News —Dr Edith Cserny has been appointed superintendent of Huntington State Hospital The appointment, announced by Dr Robert P Hagerman, director of the State Department of Mental Health, was effective July 18 Dr Cserny was appointed acting superintendent of the institution in June, 1959 Previously, she had been serving as psychiatrist and member of the medical staff —— Dr Edward A Litsinger, formerly of Charleston has been appointed by Governor Cecil H Underwood as superintendent of Spencer State Hospital The appointment was effective July 1 He has served as acting superintendent since April 1, 1959, succeeding Dr Isaac C East, Spencer

GENERAL

Medical Writers Change Meeting Dates —Dr Austin Smith, Washington, D C , president, American Medical Writers Association, announced that the meeting of the association originally scheduled for Sept 30 Oct 1, has been changed to Nov 18-19 The meeting will be held in Chicago For information, write Dr Harold Swanberg, 510 Maine St Quincy, Ill , Secretary

Blood Bank Group Meeting in San Francisco —The American Association of Blood Banks will hold its 13th annual meeting at the Jack Tar Hotel San Francisco, Aug 21-26 Major topics of scientific papers will include the importance of blood groups in transfusion therapy and their contribution to human genetics and anthropology, research advances in the preservation of whole blood and other techniques for improving this medical service, and ways of assuring adequate blood coverage for the nation Inquiries may be sent to the American Association of Blood Banks, Miss Lois James 30 N Michigan Ave , Chicago 2

Royal Society Celebrates Triennium —On the occasion of the 300th anniversary of the founding of the Royal Society of London, July 22, Detlev W Bronk, Ph D , president of the Rockefeller Institute and the National Academy of Sciences, and the King of Sweden received honorary degrees from the Queen Mother, chancellor of the University of London Others to be honored were Prof Homi Jehangir Bhabha of India, Sir Macfarlance Burnet of Australia, Prof George Charles de Hevesy, of Sweden, and Sir Thomas Merton, of England Dr Bronk has been a foreign member of the Royal Society for 12 years

Meeting of Automotive Medicine Group —The American Association for Automotive Medicine will hold its annual meeting Sept 19-20 at Dearborn, Mich The entire program will be arranged by the Ford Motor Company, which will show in detail their research and safety program The conference will include a schedule of tours, film presentations, technical lectures, and demonstrations of automotive safety engineering activities Registration for the technical sessions will be limited to physicians and special guests The annual banquet will be held at 7 30 p m , Sept 19 For information, write Dr Harold A Fenner Jr , 115 W Sanger St , Hobbs, N M , Convention Chairman

Russian Biology Translations —The American Institute of Biological Sciences, with support from the National Science Foundation, is currently translating and publishing seven Russian research journals in biology The journals currently being translated are Doklady Biological Sciences Section, Doklady Botanical Sciences Section, Doklady Biochemistry Section, Plant Physiology, Microbiology, Soviet Soil Science, and Entomological Review In addition, the A I B S has instituted a separate program of translation and publication of selected Russian monographs in biology For information, write the American Institute of Biological Sciences, 2000 P St N W , Washington 6, D C

Meeting of Orthopedists —The 48th annual meeting of the Clinical Orthopaedic Society will be held Oct 20-22 at the Schroeder Hotel, Milwaukee, with clinical sessions to be held at the Memorial Center on the Lake Sixteen clinical presentations are scheduled, with the following presented by invited speakers

Quadrilateral Socket, Dr C Hugh Hickey Shorewood, Wis
Metatarsus Primus Varus Dr James R Regan Milwaukee
Ankle Sprains—Operative Treatment Dr Owen E Miller, Milwaukee

Discussion periods are scheduled For information, write Dr Charles H Frantz, 1810 Wealthy St S E , Grand Rapids 6, Mich , Secretary-Treasurer

Research Foundation Announces Awards —The Jane Coffin Childs Memorial Fund for Medical Research announced appropriations made by its board of managers during 1959-1960 in the total sum of $371,857 for support of cancer research projects and fellowships Two such awards were $56,600 to Dr Harry S N Greene, Yale University School of Medicine, and $56,500 to Dr Leon L Miller, University of Rochester School of Medicine and Dentistry Awards were also given to Drs Osamu Hayaishi, Yukio Sugino of the department of medical chemistry, Kyoto University College of

Medicine, Japan, and Drs Itaru Watanabe and Takashi Yura, Institute for Virus Research, Kyoto University

Society News—At its annual meeting July 5 the **American Goiter Association, Inc** elected the following Dr Alexander Albert, Rochester, Minn, president, Dr Virginia Kneeland Frantz, New York City, president-elect, Dr Lindon Seed, Chicago, first vice-president, Dr Theodore O Winship, Washington, D C, reelected treasurer, and Dr John C McClintock, 702 Madison Ave, Albany 8, N Y, reelected secretary.——The **North American Chapter of the International Cardiovascular Society** had its eighth annual scientific meeting June 11 The newly elected officers are president, Dr Frank L A Gerbode, San Francisco, vice-president, Dr Jere W Lord Jr, New York City, secretary, Dr Ralph A Deterling Jr, 171 Harrison Ave, Boston 11, and treasurer, Dr William H Muller Jr, Charlottesville, Va

Report on Traffic Fatalities—Traffic accidents across the nation took a toll of 17,090 lives in the first six months of 1960, the National Safety Council reported July 28 This represented virtually no change from the toll of 17,100 deaths for the same period last year The council estimated that 600,000 persons suffered disabling injuries in the six-month period Travel was up 3% in the six months This increase combined with the unchanged death toll to produce a mileage death rate (deaths per 100 million miles of travel) of 5 0, lowest on record for the first half of any year The rate for the same period last year was 5 1 Traffic deaths in June totaled 3,320—2% more than the 3,260 in the same month last year The June increase followed rising tolls in May and April and wiped out earlier improvement

Nutrition Congress in Washington, D C—The fifth International Congress of Nutrition will be held Sept 1-7 at the Sheraton-Park and Shoreham hotels, Washington, D C A symposium, "World Food Needs and Food Resources," is planned for Sept 6 Seven panel discussions are scheduled as follows

Evaluation of Nutritional Status in Man
Proteins and Amino Acids in Nutrition
Lipids in Health and Disease
Nutrition in Maternal and Infant Feeding
Effects of Processing and Additives on Foods
Animal Nutrition and Food Production
Three Hours Around the World—New Possibilities in Nutrition Research

A social program is arranged and includes tours and special activities For information, write the Secretariat, Fifth International Congress on Nutrition, 9650 Wisconsin Ave, Washington 14, D C

Rehabilitation Fellowship to Japanese Physician—The awarding of an American President Lines' International Fellowship in Rehabilitation to Dr Hajime Ishida, Tokyo University School of Medicine, was announced Dr Ishida will be provided a minimum of one year of postgraduate training in physical medicine and rehabilitation in the United States He holds a degree of Ph D as well as M D and has been a member of the staff of the department of orthopedics, Tokyo University School of Medicine, since 1953 Dr Ishida will begin his American President Lines' International Fellowship in Rehabilitation at the Institute of Physical Medicine and Rehabilitation, New York University Medical Center, in August He will also represent Japan at the eighth World Congress of the International Society for the Welfare of Cripples, New York City, Aug 28-Sept 2

Meeting on Medical Clinics Group—The American Association of Medical Clinics will hold its 11th annual session Oct 6-8 in New Orleans Workshops will be held Oct 7 under the following titles Partnerships and Associations (Pros and Cons), Family or General Practice in Clinics, and Radioisotopes Guest speakers at the luncheon Oct 7 and 8 will be Alexander Sas-Jaworsky, D V M, Abbeville, La, and Dr Norbert J Roberts, associate medical director, Standard Oil Company (New Jersey), New York City Three panel discussions are planned for Oct 8 Labor's Medical Care Desires and Accomplishments, Problems in Graduate and Postgraduate Medical Education, and Insurance and Retirement Programs for Clinics Technical exhibits are arranged For information, write Dr Edwin P Jordan, Box 58, Charlottesville, Va, Executive Director

Northwest Meeting on Occupational Medicine—On Sept 11, the annual meeting of the Northwest Association of Occupational Medicine will be held at the Hotel Multnomah, Portland, Ore A clinic on industrial dermatoses for nurses only will be conducted by Dr Donald J Birmingham, Cincinnati, during the morning session The program includes the following topics and speakers

Etiology of Disease—Single vs Multiple Causation, Dr James S Tyhurst, Vancouver, British Columbia
Enzymes, Key to Cellular Existence, Wilbert R Todd, Ph D, Portland
Heavy Metal Poisoning, Dr Charles M McGill, Tacoma, Wash
Prelude to Litigation, Herbert Schuab, judge, Circuit Court of Oregon, Portland
What is Preventable? Dr Norbert J Roberts, Standard Oil Co, New Jersey
Troubled Breathing, Dr Donald M Pitcairn, Portland
Pneumoconioses—Real and Rumored, Dr Oscar A Sander, Milwaukee
Life Span Immunization, Dr Howard L Reed, Wilmington, Del
Spoxy Resins and the Patch Test, Dr Birmingham

President of the association is Dr William D Norwood, Richland, Wash, program chairman is Dr. Forrest E Rieke For information, write Dr Rieke at 1313 N W 19th Ave, Portland 9, Ore

Prevalence of Poliomyelitis —According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated

Area	July 16 1960 Paralytic Type	July 16 1960 Total Cases	July 18 1959 Total
New England States			
Maine			
New Hampshire			
Vermont			
Massachusetts			1
Rhode Island	18	24	
Connecticut	1	1	4
Middle Atlantic States			
New York	3	3	9
New Jersey	1	2	1
Pennsylvania	3	5	
East North Central State			
Ohio			5
Indiana	1	1	3
Illinois	5	7	7
Michigan		2	6
Wisconsin			
West North Central States			
Minnesota			5
Iowa		1	19
Missouri	1	2	32
North Dakota			
South Dakota			
Nebraska	1	1	8
Kansas			5
South Atlantic States			
Delaware			
Maryland			
District of Columbia			
Virginia			8
West Virginia		1	6
North Carolina			6
South Carolina	7	12	1
Georgia			6
Florida	2	2	7
East South Central States			
Kentucky			
Tennessee	1	1	12
Alabama	4	4	1[illegible]
Mississippi	1	1	3
West South Central States			
Arkansas	2	3	11
Louisiana	2	3	5
Oklahoma	1	1	9
Texas	2	5	34
Mountain States			
Montana			
Idaho			1
Wyoming			
Colorado			2
New Mexico			4
Arizona			4
Utah			
Nevada			1
Pacific States			
Washington			3
Oregon			5
California	12	12	7
Alaska			
Hawaii	1	1	
Territories and Possessions			
Puerto Rico	19	19	
Total	88	114	2[illegible]

Military Surgeons Meeting in Washington, D C —The 67th annual convention of the Association of Military Surgeons will be held Oct 31-Nov 2 in Washington, D C The theme of the convention is The Military Role in Medical Progress" Rear Admiral Richard A Kern, MC, USNR, president of the association, will open the meeting on Oct 31 On Tuesday afternoon, Nov 1, the William C Porter Lecture will be presented by Dr Manfred S Guttmacher, chief medical officer of the Medical Service of the Supreme Bench of Baltimore The Porter Lecture, sponsored by the Smith Kline and French Laboratories of Philadelphia to honor a pioneer in military psychiatry, was established in 1958 Following the Porter Lecture there will be a panel discussion on cholera, with the following papers presented Physiological Abnormalities and Their Therapeutic Correction', Pathogenesis as Revealed by Intestinal Biopsy , Immunological Approaches to Control', and 'Review of the SEATO Cholera Research Program' A panel, Man and the Radiation Hazard," will cover the afternoon program Nov 2 During the three-day meeting there will be special section meetings with panel discussions for the dentists, nurses, medical specialists, and veterinarians Films on medical and scientific subjects will be shown There will be various technical and scientific exhibits Reserve officers attending the meeting may register for credit points There is no registration fee, nonmembers are invited For information, write the Association of Military Surgeons, 1726 Eye St, N W, Washington 6, D C

Oral Cancer Conference in Phoenix —The American Society of Oral Surgeons will sponsor a "Conference on Oral Cancer" Tuesday, Oct 11, at the Westward Ho Hotel, Phoenix, Ariz The conference precedes the society's 42nd annual meeting and is offered under a grant by the National Institute of Dental Research Cooperation and participation is being invited among medical and dental groups of the Southwest The conference program includes a motion picture, "Surgical Treatment of Pre-Cancerous Lesions,' by Col Robert B Shira, Walter Reed Hospital, Washington, D C Five papers are scheduled for presentation as follows

The Role of the Oral Pathologist in the Diagnosis of Oral Lesions, Major Surindar N Bhaskar D D S Washington, D C
Activity of the Schools of Dentistry in Graduate and Post-Graduate Training for Early Detection of Oral Cancer, Hamilton B G Robinson D D S, Kansas City Mo
The Effect of Environment on Cancer Incidence Dr Ernest L Wynder, New York City
Newer Modalities in Radiation Therapy—A Discussion Dr Gilbert H Fletcher, Houston, Texas
A Two Year Review of Research in Cancer Etiology at the Sloan-Kettering Institute Chester Stock Ph D New York City

The proceedings of the conference will be published For information, write the American Society of Oral Surgeons, Mr D C Trexler, Executive Secretary, 840 N Lake Shore Drive, Chicago 11

LATIN AMERICA

Symposium on Rheumatic Diseases in Mexico —The Pan American Medical Association and the Mexican League Against Rheumatism are organizing a symposium, 'Present Status of Clinical and Therapeutic Knowledge of Some Rheumatic Diseases, to be held in Ixtapan, Mexico, Oct 19-23 Gout, rheumatic fever, rheumatoid arthritis, and other connective tissue diseases will be considered under the general headings, Treatment with Corticosteroids" and Clinical and Therapeutic Recent Advances Drs Maxwell Lockie, Joseph Bunim, and Richard Freyberg are among those taking part in the lectures and discussions, all of which are to be in English Travel arrangements and tours are being taken care of by General Tours, Inc, 595 Madison Ave, New York 22, N Y from whom additional information concerning the scientific program may be obtained

CORRECTIONS

Photomicrographs Reversed—In the article, "Duplication of the Rectum Containing Gastric Mucosa," on page 1224, July 16 issue of The Journal, the two photomicrographs presented as figure 3 should be reversed

French Polynesia—In The Journal, May 28, 1960, page 358, in the fifth line from the end of the contribution, "Outbreak of Typhoid Fever Starting with A Case of Purulent Meningitis" the words "French Indonesia" should have been "French Polynesia"

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology *Written* Various locations, June 30 Sec, Dr Forrest E Leffingwell, 217 Farmington Ave, Hartford 5, Conn

American Board of Dermatology Final date for filing applications of candidates completing training by October 15, 1960 is March 1, 1961 *Written* Several cities, June 5, 1961 *Oral* Philadelphia, Oct 13-16, 1961 Sec, Dr Maurice J Costello, One Haven Avenue, New York 32, New York

American Board of Internal Medicine New York City, Nov 14-17 Closing date for filing application was July 1 *Written* Oct 17 Closing date for filing application was May 1 Schedule for 1961 *Written Examination*, October 16 *Oral Examinations* New Orleans, Jan 30-Feb 2, Chicago, April 4-7, Los Angeles, Sept 26-29, New York City, Nov 7-10 Closing date for acceptance of applications for the January and April examinations is October 1, 1960, and for the September and November examinations is June 1, 1961 Sec-Treas, Dr William A Werrell, One West Main St, Madison 3, Wis

American Board of Neurological Surgery *Oral* New Haven, Nov 13-16 Final date for filing application is Sept 1 Sec, Dr Donald D Matson, 300 Longwood Ave, Boston 15

American Board of Obstetrics and Gynecology *Written* Various cities of the United States, Canada, and military centers outside of continental United States, January 13 *Oral* Chicago, Apr 7-14 Application for certification, new and reopened in Part I, and requests for reexamination in Part II are now being accepted Deadline for receipt of applications for the written examination is August 1 Candidates submitting applications in 1960 for the 1961 examinations are not required to submit case reports as previously required to complete the Part I examination In lieu of this requirement, new candidates are required to keep in their files a duplicate list of hospital admissions as submitted with their application, for submittal at the annual meeting in Chicago should they become eligible to take the Part II (oral) examination Reopened candidates will be required to submit case reports for review thirty days after *notification* of eligibility Exec Sec, Dr Robert L Faulkner, 2105 Adelbert Road, Cleveland 6

American Board of Ophthalmology *Written* Jan 23, 1961 Deadline for filing applications was July 1 *Oral* Chicago, Oct 3-7 Sec, Dr Merrill J King, Box 236 Cape Cottage Branch, Portland, Maine

American Board of Orthopaedic Surgery *Written, Part I* Palo Alto, Calif, Nashville, Tenn, Philadelphia, June 19-20 Final date for filing application is Nov 30 *Oral, Part II* Miami Beach, Jan 4-6 Final date for filing application was July 1 Sec, Dr Sam W Banks, 29 E Madison St, Chicago 2

American Board of Otolaryngology *Oral* Chicago, Oct 3-6 Final date for filing application was April 1 Sec, Dr Dean M Lierle, University Hospitals, Iowa City

American Board of Pathology *Examination* Indianapolis, Oct 20-22 Final date for filing application is Sept 15 Sec, Dr Edward B Smith, 1100 W Michigan St, Indianapolis 7

American Board of Pediatrics *Oral* Chicago, Oct 21-23 Final date for filing application has passed *Written* New York City, January Final date for filing application is Dec 1 Sec, Dr John McK Mitchell, 6 Cushman Road, Rosemont, Pa

American Board of Plastic Surgery Entire examination—*written*, and *oral* and *practical* given in May of each year Final date for submitting case reports is November 1 Next examination to be given in New York City, May 1961 Corres Sec, Mrs Estelle E Hillerich, 4647 Pershing Ave, St Louis 8, Mo

American Board of Proctology *Oral and Written, Parts I and III* Philadelphia, Sept 17 Final date for filing application was June 30 Sec, Dr Stuart T Ross, 520 Franklin Ave, Garden City, N Y

American Board of *Psychiatry and Neurology* New York, New York, Dec 12-13, New Orleans, Mar 20-21, and Chicago, Oct 9-10, 1961 Sec, David A Boyd, Jr, 102-110 Second Ave, S W, Rochester, Minn

American Board of Radiology *Examination* Cincinnati, Dec 10-13 Deadline for filing applications for the June examination was Jan 1 Filing deadline for the December examination was July 1 A special *examination in* Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications Sec, Dr H Dabney Kerr, Kahler Hotel Bldg, Rochester, Minn

American Board of Surgery *Written* (Part 1), Various Centers, Dec 7 *Candidates are urged to apply several months before completion of training requirements* The closing date for filing applications is August 1 Those completing training requirements after September 30 cannot be considered for the December Part I examination of the same year *Oral* (Part II)—New Haven, Sept 26-27, Indianapolis, Oct 24-25, Buffalo, Nov 14-16, Nashville, Dec 12-13, Philadelphia, Jan 16-17, Houston, Feb 13-14, Columbus, Ohio, Mar 13-14, New York City, April 19 20, Portland, Ore, May 15-16, San Francisco, May 18-19 No examinations will be held in June, July or August Sec-Treas, Dr John B Flick, 1617 Pennsylvania Blvd, Philadelphia 3

Board of Thoracic Surgery *Written* Various centers throughout the country, Sept 9 Final date for filing application was July 1 *Oral* Oct 1960 *Final* date for filing application is July 1 Sec, Dr Wm M Tuttle, 1151 Taylor Ave, Detroit 2

American Board of Urology *Written* December *Oral Clinical* Chicago, February 1961 Exec Sec, Mrs Ruby L Griggs, 30 Westwood Road, Minneapolis 26

DEATHS

Adams, Fletcher Ruff Ⓜ Concord, N C, Medical College of the State of South Carolina, Charleston, 1935, served as health officer of Union and Catawba counties, on the staff of the Veterans Administration Hospital in Salisbury, where he died May 1, aged 53, of hemopericardium

Adler, Ilka Wilheim, Cleveland, Medizinische Fakultat der Universitat, Vienna, Austria, 1921, specialist certified by the American Board of Psychiatry and Neurology, member of the American Psychiatric Association, director of Harmony Hall and senior staff psychiatrist at the Cleveland State Hospital, died in the Mount Sinai Hospital May 17, aged 64, of embolism and pulmonary emphysema

Anderson, Daniel Herbert, Chicago, Northwestern University Medical School, Chicago, 1902, on the staff of the Provident Hospital, died May 2, aged 84, of cancer

Arveson, Raymond Gregory, Frederic, Wis, Wisconsin College of Physicians and Surgeons, Milwaukee, 1906, fellow of the American College of Surgeons, in 1957 was given the Council Award of the State Medical Society of Wisconsin, of which he was past-president, for many years village president of Frederic and village supervisor, served on the school board, at one time a member of the state board of medical examiners, associated with the Frederic Municipal Hospital, formerly regent of the University of Wisconsin in Madison, died June 5, aged 76, of cerebral hemorrhage

Balko, Andrew John Ⓜ Long Island City, N Y, St Louis University School of Medicine, 1934, veteran of World War II, associated with Forest Hills (N Y) General Hospital and the Boulevard Hospital, died May 31, aged 52, of coronary sclerosis

Bates, Floyd Robert Ⓜ Walton, N Y, Syracuse University College of Medicine, 1930, member of the American Academy of General Practice, on the staff of the Delaware Valley Hospital, died in the Homer Folks Tuberculosis Hospital, Oneonta, May 20, aged 64, of pulmonary tuberculosis and chronic lymphocytic leukemia

Belknap, Horace Preston Ⓜ Nampa, Idaho, University of Oregon Medical School Portland, 1916, veteran of World War I, in 1938 a representative of Canyon County to the Idaho Legislature, on the staff of the Mercy Hospital, past-president of the Rotary Club, died May 19, aged 70, of coronary occlusion

Berk, Lester Ivin, Miami Beach, Fla, University of Pittsburgh School of Medicine, 1943, formerly an officer in the medical corps, Army of the United States, interned at the Presbyterian Hospital in Pittsburgh, died May 20, aged 44, of myocardial infarction

Bessette, Adelard Elphige, Belen, N M, Rush Medical College, Chicago, 1902, died in Albuquerque June 7, aged 86, of cerebral arteriosclerosis

Black, Forest A, Seattle, Vanderbilt University School of Medicine, Nashville, Tenn, 1905, veteran of World War I, died June 4, aged 79, of coronary thrombosis

Blanchard, Thomas Washington Ⓜ Hobbsville, N C, Medical College of Virginia, Richmond, 1911, a director of the Bank of Hobbsville, died in the Louise Obici Memorial Hospital, Suffolk, May 20, aged 77, of coronary thrombosis

Boreen, Clifton A Ⓜ Minneapolis, University of Minnesota College of Medicine and Surgery, Minneapolis, 1909, veteran of World War I, died in Long Lake May 1, aged 77, of arteriosclerosis

Bradley, Millard Calvin Ⓜ Compton, Calif, College of Medical Evangelists, Loma Linda and Los Angeles, 1937, certified by the National Board of Medical Examiners, died in San Francisco April 4, aged 53, of coronary occlusion

Butler, John Oscar, Guthrie, Okla, Marion-Sims College of Medicine, St Louis, 1896, died Feb 17, aged 85, of cerebral hemorrhage

Cangelosi, Joseph Peter Ⓜ Oak Park, Ill, Chicago Medical School, 1936, interned at the Cook County Hospital in Chicago, senior surgeon, St Elizabeth Hospital in Chicago, died in St Marys Hospital, Rochester, Minn, May 30, aged 52, of carcinoma of the common bile duct

Cannon, Joseph Henry, Charleston, S C, born in Charleston Nov 1, 1886, Medical College of South Carolina, Charleston, 1912, specialist certified by the American Board of Internal Medicine, fellow of the American College of Physicians, member of the House of Delegates of the American Medical Association from 1926 through 1941 and in 1943 past-president of the Medical Society of South Carolina and treasurer of that organization for many years, for many years on the faculty of his alma mater, veteran of World War I, on the staffs of Roper Baker, and St Francis hospitals, died May 22 aged 73 of cancer

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Ⓜ Indicates Member of the American Medical Association

Carroll, William A Ⓜ Claude, Texas, University of Tennessee Medical Department, Nashville, Tenn, 1901, died in Amarillo April 22, aged 85, of cerebral hemorrhage

Case, Otis Jameson, Salamanca, N Y, New York Homeopathic Medical College and Hospital, New York City, 1907, veteran of World Wars I and II, served on the staffs of the St Francis Hospital in Olean, Edward J Meyer Memorial Hospital, Millard Fillmore Hospital, Lafayette General Hospital, and Buffalo General Hospital in Buffalo, and the Salamanca District Hospital, where he died May 15, aged 77, of cerebral metastasis

Clayton, E Harry, Arkansas City, Kan, College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908, veteran of World War I, on the staff of the Arkansas City Memorial Hospital, where he died May 10, aged 79 of coronary occlusion

Cooper, Frederick Sturges, Rocky River, Ohio, Columbia University College of Physicians and Surgeons, New York City, 1912, died March 19, aged 72, of leukemia and pneumonia

Crews, Numa Haden Ⓜ Greeneville, Tenn, Jefferson Medical College of Philadelphia, 1914, veteran of World War I, died May 11, aged 71, of coronary thrombosis

Crow, Emory Speer Ⓜ Olustee, Okla, University of Georgia Medical Department, Augusta, 1902, died in the Jackson County Memorial Hospital, Altus, June 1, aged 82, of cerebrovascular disease

Daines, Orson Suel Ⓜ Ogden, Utah, Northwestern University Medical School, Chicago, 1931, associated with the St Benedict's Hospital and the Thomas D Memorial Hospital, where he died May 28, aged 56, of uremia

Danos, Joseph Louis, Thibodaux, La, Medical Department of Tulane University of Louisiana, New Orleans, 1903, honorary president of Lafourche National Bank, honorary member of the medical staff at St Joseph Hospital, where he died May 31, aged 80, of uremia and general arteriosclerosis

Delph, Walter Ivey, New York City, Howard University College of Medicine, Washington, D C, 1922, associated with the Sydenham Hospital, where he died May 29, aged 65, of cancer

De Porte, Seymour, Oklahoma City, Okla, University of Oklahoma School of Medicine, Oklahome City, 1919, died Feb 5, aged 74, of coronary infarction

Diehl, Reuben Oscar, Manheim, Pa, Hahnemann Medical College and Hospital of Philadelphia, 1905, associated with Lancaster General and St Joseph's hospitals in Lancaster, for many years served on the board of directors of the Keystone National Bank, died May 22, aged 86, of coronary occlusion

Diven, George Raphield, Los Angeles, College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901, member of the honorary staff of St Vincent's Hospital, died June 5, aged 84, of carcinoma of the bladder and uremia

Donaldson, Henry Clay, Robinsonville, Miss, Memphis (Tenn) Hospital Medical College, 1908, died in Meridian May 14, aged 78, of arteriosclerosis

Donohoe, Hobart Lewis Ⓜ Columbus, Ohio, Ohio State University College of Medicine, Columbus, 1931, member of the American Academy of General Practice and the Columbus Academy of Medicine, veteran of World War I, affiliated with St Ann's, Grant, White Cross, Mercy, and St Anthony's hospitals, died in the University Hospital May 19, aged 62, of lymphosarcoma

Dry, Frank Mortimer Ⓜ Chicago, Loyola University School of Medicine, Chicago, 1918, member of the American Academy of General Practice, served on the faculty of Northwestern University Medical School from 1928 to 1930, member of the staff of the Augustana Hospital, where he died May 23, aged 66, of bronchopneumonia

Dudding, Joseph Eastman Ⓜ Hope, Ind, Indiana University School of Medicine, Indianapolis, 1935, formerly county coroner, served on the staffs of the Bartholomew County Hospital in Columbus, Major Hospital in Shelbyville, and Methodist Hospital in Indianapolis, died in the Marion County General Hospital in Indianapolis May 20, aged 53, of dissecting aortic aneurysm

Duenner, Robert Henry, Colonel, U S Army, retired, Newark, Del, George Washington University School of Medicine, Washington, D C, 1910, entered the medical corps of the U S Army in 1913, veteran of World Wars I and II, retired Nov 30, 1946, director of student health at the University of Delaware, died in the Walter Reed General Hospital, Washington, D C, June 12, aged 77, of myelofibrosis due to polycythemia vera

Dugan, William Miller Ⓜ Indianapolis, born July 11, 1904, Indiana University School of Medicine, Indianapolis, 1929, member of the American Rheumatism Association, fellow of the American College of Physicians, served as secretary of the Indianapolis Medical Society and the Indianapolis Diabetic Association, served as physician for the Civil Aeronautics Administration, member and past president of the staff of the Methodist Hospital, past-president of the staff of the Indianapolis General Hospital, member of the staffs of St Vincent's and Community hospitals, and Indiana University Medical Center, on the board of the Marion County Tuberculosis Hospital in Sunnyside, died May 19 aged 55, of massive cerebral hemorrhage

Elmendorf, John Edward Jr, New York City, born May 28, 1893, Johns Hopkins University School of Medicine, Baltimore, 1918, joined the International Health Division of the Rockefeller Foundation in 1920 and until 1936 served the division in Costa Rica, Venezuela, Brazil, and in the division laboratories in New York, in 1937 organized and directed a malarial control study in Pensacola, Fla, and Escambia County, in 1941 was transferred to Jacksonville, Fla, where he became director of the Bureau of Malaria Control of the Florida Board of Health, in 1942, at the request of the Army, the bureau organized and conducted training courses in malaria field investigation and control procedures for Army officers, and he directed these courses, in 1943 on leave of absence from the International Health Division, served with the Army as commandant of the Army School of Malariology in the Panama Canal Zone, in 1946 left the Army with the rank of colonel and was awarded the Legion of Merit in the same year, the following year returned to the International Health Division and served as director of Carlos Finlay Yellow Fever Institute, Bogota, Colombia, South America, until 1951 when he became scientific director of the National School of Hygiene in Colombia, which he planned and organized, retired in 1953 as a member of the staff of the division of public health of the Rockefeller Foundation, decorated by the British, Colombian, and Mexican governments, served on the National Resources Planning Board, certified by the National Board of Medical Examiners, fellow of the American Association for the Advancement of Science, American Public Health Association, New York Academy of Medicine, and the American Society of Tropical Medicine and Hygiene, died in Johns Hopkins Hospital, Baltimore, May 25, aged 66, of internal hemorrhage from abdominal aorta, nontraumatic

Fehr, Allen F, Palmerton, Pa, Middlesex College of Medicine and Surgery, Cambridge, Mass, 1917 died in the Palmerton Hospital May 29, aged 77 of cerebrovascular accident

Finley, H Webb, Lubbock, Texas, University of Oklahoma School of Medicine, Oklahoma City, 1912, died in the Emory John Brady Hospital, Colorado Springs, Colo May 7, aged 76 of arteriosclerotic heart disease

Fletcher, William R Ⓜ Joliet, Ill, Kentucky School of Medicine, Louisville, 1900, physician and surgeon with the Illinois State Penitentiary for 20 years, postmaster from 1927 to 1933 and for many years county physician, served overseas during World War I, past-president of the Will-Grundy Counties Medical Society, on the staffs of Silver Cross Hospital and St Josephs Hospital, where he died May 20, aged 83, of hypostatic pneumonia

Flynn, John F, Bridgeport, Conn, College of Physicians and Surgeons, Baltimore, 1911, served as a member and president of the city board of health, formerly police surgeon, associated with the Bridgeport Hospital, died May 21, aged 74, of acute coronary occlusion

Forney, Lee Ole Ⓜ Hutchinson, Kan, Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1905, for many years county health officer, associated with St Elizabeth Hospital and Grace Hospital, where he died May 25, aged 88, of cerebral thrombosis

Foshay, Lee, Cincinnati, born in Cleveland Jan 20, 1896, University of Pennsylvania School of Medicine, Philadelphia, 1920, certified by the National Board of Medical Examiners, member and past-president of the Central Society for Clinical Research, professor of microbiology and head of the department at the University of Cincinnati College of Medicine, formerly on the faculty of Western Reserve University School of Medicine in Cleveland and the State University of Iowa College of Medicine in Iowa City, died in the Holmes Hospital June 6 aged 64, of amelanotic melanoma with diffuse metastasis

Foshee, Reuben Aaron, Alexander City, Ala, University of Alabama Medical Department, Mobile, 1907, died May 17, aged 78, of carcinoma of the pharynx

Garabedian, Noubar Joseph Ⓜ Staten Island, N Y, born in Adana, Turkey, March 5, 1919, Georgetown University School of Medicine, Washington, D C, 1943, certified by the National Board of Medical Examiners, specialist certified by the American Board of Obstetrics and Gynecology, interned at the Fordham Hospital in New York City and the Long Island College Hospital in Brooklyn, where he served a residency, served on the staffs of the Brooklyn Cancer Institute, Long Island College Hospital, and the Kings County Hospital in Brooklyn, chief obstetrician at the Staten Island Medical Center, died in St Vincents Hospital June 7 aged 41, of duodenal ulcer

Gay, Lee Pettit Ⓜ Jefferson City, Mo, born in Ironton, Aug 2, 1894, Washington University School of Medicine, St Louis, 1918, at one time on the faculty of his alma mater, specialist certified by the American Board of Internal Medicine, fellow of the American College of Physicians, member of the American College of Allergists and of the Missouri Historical Society, veteran of World Wars I and II, on the staff of St Marys Hospital, for many years practiced in St Louis, where he was chief of the medical staff at St Louis County Hospital and a visiting staff member at St Lukes, Barnes, and the Frisco Employes' hospitals, died while attending a medical meeting in Barcelona, Spain, June 1, aged 65, of coronary disease.

Glasser, Robert Daniel, Norfolk, Va., Medical College of Virginia, Richmond, 1912; member of the Southeastern Surgical Congress; on the staffs of the De Paul Hospital, Leigh Memorial Hospital, and the Norfolk General Hospital, where he died May 21, aged 73, of coronary insufficiency.

Goldberg, Milton Harry Ⓜ Buffalo; University of Buffalo School of Medicine, 1912; served in France during World War I; died in the Millard Fillmore Hospital May 29, aged 72, of coronary thrombosis.

Gottlieb, Charles Ⓜ New York City; born Sept. 8, 1886; University and Bellevue Hospital Medical College, New York City, 1907; specialist certified by the American Board of Radiology; member of the American College of Cardiology, American College of Chest Physicians, and the American College of Radiology; professor emeritus of radiology at his alma mater, now known as the New York University College of Medicine; consultant at the Gouverneur Hospital and the University Hospital; died in the Manhattan General Hospital June 5, aged 73, of myocardial infarction.

Gratz, Raymond Joseph, Indianapolis; Washington University School of Medicine, St. Louis, 1951; interned at George Washington University Hospital in Washington, D. C.; served a residency at the Brooklyn Hospital and the Veterans Administration Hospital in Richmond, Va.; served as an officer in the medical corps of the U. S. Air Force Reserve; died in Barnes Hospital, St. Louis, May 16, aged 38, of cancer of the right lung.

Hagans, Frank Marion, Lincoln, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1905; past-president of the Logan County Medical Society; veteran of World War I; on the staffs of the Abraham Lincoln Memorial Hospital and St. Clara's Hospital, where he died June 2, aged 79, of coronary occlusion.

Herdien, Elmer Forrest Ⓜ Watseka, Ill.; Northwestern University Medical School, Chicago, 1901; member of the American Association of Railway Surgeons; veteran of World War I; served on the staff of the Iroquois Hospital, where he died May 27, aged 84, of acute pulmonary edema.

Hines, John Howard Ⓜ Roswell, Ga.; Emory University School of Medicine, Atlanta, 1937; interned at the Grady Hospital; served a residency at St. Joseph Infirmary in Atlanta; member of the American Academy of General Practice; formerly practiced in Atlanta, where he was on the staff of the Crawford W. Long Memorial Hospital, where he died May 28, aged 51, of uremia.

Hooker, Henry Frost, Danville, Ill.; Northwestern University Medical School, Chicago, 1908; fellow of the American College of Surgeons; member of the Industrial Medical Association; member and past-president of staffs, St. Elizabeth and Lake View hospitals; associated with Danville Polyclinic, of which he was a founder; died May 19, aged 79, of carcinoma.

Hunt, William Bryce, Lexington, N. C.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1923; formerly mayor; died May 18, aged 64, of coronary heart disease.

Hussey, Earle Ulmont, Lynn, Mass.; Boston University School of Medicine, 1917; veteran of World Wars I and II; associated with the Union Hospital and the Lynn Hospital, where he died May 14, aged 69, of ruptured aortic aneurysm.

Johnston, Charles George Ⓜ Detroit; born in St. Louis March 13, 1899; Washington University School of Medicine, St. Louis, 1926; certified by the National Board of Medical Examiners; member of the founders group of the American Board of Surgery; member of the American Surgical Association, Western Surgical Association, of which he was past-president, International Society of Surgery–American Branch, American Association for the Surgery of Trauma, of which he was past president, vice-president, and secretary, and the Central Society for Clinical Research; fellow of the American College of Surgeons; veteran of World War II; professor of surgery at Wayne State University College of Medicine, where he served as chairman of the department; at one time on the faculty of the University of Pennsylvania School of Medicine in Philadelphia; director of surgery, City of Detroit Receiving Hospital; chief of surgery, Veterans Administration Hospital in Dearborn; consulting surgeon at the Jennings Memorial and Detroit Memorial hospitals; a member of the city plan commission; died June 3, aged 61, of a heart attack.

Kardys, John Albert, Hartford, Conn.; George Washington University School of Medicine, Washington, D. C., 1930; physician at the Hartford County Jail for many years; on the staff of St. Francis Hospital; died May 28, aged 55, of coronary thrombosis.

Kass, Herman, New York City; New York University College of Medicine, 1939; veteran of World War II; member of the Industrial Medical Association; died April 18, aged 49, of coronary occlusion.

Kattus, Joseph Henry Ⓜ Cincinnati; St. Louis University School of Medicine, 1923; veteran of World War II; on the staff of St. Mary's Hospital, where he died May 31, aged 62, of embolus to the femoral artery and auricular fibrillation.

King, Frank Chapman, Washington C H, Ohio, Ohio State University College of Medicine, Columbus, 1952, interned at the Grant Hospital in Columbus, Ohio, associated with the Fayette County Memorial Hospital, died May 19, aged 38, of coronary occlusion

Kubista, Anna, Scotch Plains, N J, New York Medical College and Hospital for Women, Homeopathic, New York, 1911, died in the Muhlenberg Hospital, Plainfield, May 19, aged 78, of cerebral hemorrhage

Lawrence, Oscar Victor, Brownsville, Texas, University of Texas School of Medicine, Galveston 1907, served on the school board, on the staff of the Mercy Hospital, died May 27, aged 84, of pneumonia

Lindsay, Merrill Kirk Ⓜ New Haven, Conn, born in Topeka, Kan, May 20, 1884, Columbia University College of Physicians and Surgeons, New York City, 1910, specialist certified by the American Board of Orthopaedic Surgery, member of the American Orthopaedic Association, fellow of the American College of Surgeons, formerly on the faculty of Yale University School of Medicine, served in the regular Army, veteran of World War I, retired in 1954 as orthopedist with the Veterans Administration in Washington, D C, died in the Veterans Hospital, West Haven, May 24, aged 76 of septicemia due to Escherichia *coli*, cerebral arteriosclerosis

Lubin, Philip Ⓜ Brooklyn, University and Bellevue Hospital Medical College, New York City, 1918, veteran of World War I, died in the Maimonides Hospital May 25, aged 63, of uremia

McCall, William Reed Ⓜ La Grange, Ga, Medical College of Virginia, Richmond, 1905, member of the American Society of Anesthesiologists, on the staff of the City-County Hospital, where he died May 27, aged 79, of myocardial infarction

MacLeod, Johnston Ⓜ Flushing N Y, Bellevue Hospital Medical College, New York City, 1891, veteran of World War I, on the staff of the Flushing Hospital, died May 23, aged 92, of cerebral hemorrhage

Maguire, Vincent de Paul, Wilmington, Del, University of Pennsylvania School of Medicine, Philadelphia, 1943, interned at the Delaware Hospital, where he was a member of the staff, veteran of World War II, associated with the Wilmington General Hospital and St Francis Hospital where he died May 20, aged 41, of acute coronary thrombosis

Maxwell, James Hoyt, Ann Arbor, Mich, born in Paw Paw, Mich Dec 15, 1901, University of Michigan Medical School, Ann Arbor 1927, professor and chairman of the department of otolaryngology at his alma mater, member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological Association, of which he was vice-president, American Laryngological, Rhinological and Otological Society, and the American Otological Society, specialist certified by the American Board of Ootolaryngology, fellow of the American College of Surgeons, on the staffs of the University and St Joseph's Mercy hospitals, died June 2, aged 58, of coronary thrombosis

Orr, August Costello Ⓜ Bismarck, N D, Rush Medical College, Chicago, 1934, served as secretary of the North Dakota Society of Obstetrics and Gynecology, formerly director of the child hygiene division of the North Dakota State Department of Health and director of the sixth district of the Michigan State Department of Health with headquarters in Newberry, county health officer, on the staff of St Alexius Hospital, died May 22, aged 57, of a heart attack

Ottinger, Ross Clement Ⓜ Indianapolis, Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907, served on the faculty of the Indiana University School of Medicine, fellow of the American College of Surgeons, veteran of World War I, on the staff of St Vincent's Hospital and Methodist Hospital, where he died May 24, aged 77, of generalized arteriosclerosis

Pascale, Vincenzo, New York City, Columbia University College of Physicians and Surgeons, New York City, 1910, for forty years was associated with the Social Hygiene Division of the Bureau of Preventable Diseases of the New York City Health Department, veteran of World War II, served on the courtesy staff of the Lawrence Hospital, Bronxville, where he died June 1, aged 73, of generalized peritonitis due to perforated duodenal ulcer

Patton, Leslie Endicott Ⓜ St Louis, St Louis University School of Medicine, 1924, associated with St Joseph Hospital in Kirkwood, St Luke's Hospital, Barnes Hospital, Jewish Hospital, and Deaconess Hospital, where he died May 28, aged 64, of cardiac insufficiency

Pence, Benjamin Franklin Ⓜ Hollywood, Fla, Indiana University School of Medicine, Indianapolis, 1915, at one time practiced in Columbia City, Ind, and served as president of the Whitley County Medical Society, veteran of World Wars I and II, died in the Memorial Hospital May 11, aged 71 of arteriosclerotic heart disease

Plummer, David Edwin, Thomasville N C, Medical College of Virginia, Richmond 1934, veteran of World War II, county coroner, died in the Veterans Administration Hospital, Durham, May 13 aged 51, of hypertensive cardiovascular disease and renal failure

FOREIGN LETTERS

FRANCE

Kanamycin for Tuberculosis—G Brouet and co-workers (*Rev tuberc pneumologie*, vol 23, 1959) reported that kanamycin was much less effective than isoniazid in guinea-pigs and mice having tuberculosis They also treated a series of 70 patients who were divided into two groups One group consisted of 24 patients who were given 0 5 Gm of kanamycin intramuscularly twice daily The other 46 patients were given kanamycin sulfate, which was combined with isoniazid for those with new and with ethienomide for those with long-standing tuberculosis In the first group, satisfactory results were obtained in 25% of the patients, in the second group, the results were better in patients with new than in those with long-standing tuberculosis

The new antibiotic was well tolerated and did not cause any disturbance on the hepatobiliary function or on hematopoiesis, but it had a toxic effect on the kidneys Severe cochlear disturbances may appear suddenly, especially in older patients Because of its toxicity, this antibiotic is indicated only for patients in relapse, for resistance to streptomycin therapy, and for severe recent tuberculosis associated with widespread open lesions Kanamycin delays the development of those strains which are resistant to isoniazid therapy

Crush Injuries—J Mirouze and co-workers (*Presse méd*, April 16, 1960) reported a series of 69 patients with kidney diseases, all victims of the Agadir catastrophy, who were hospitalized at Casablanca Nephropathies resulted from prolonged compression of certain muscles of the body, particularly those of the extremities, the face, and the lumbar region Of all those injured in Agadir, 16% suffered muscular lesions due to compression, and 69 (the present series) had post-traumatic kidney insufficiency Diffuse muscular injury and dehydration aggravated the patients' condition The first symptom of acute renal insufficiency due to trauma manifested itself by myohemoglobinuria The urine was the color of coffee grounds but contained no erythrocytes The authors differentiated three forms of kidney disease according to the degree and severity of kidney insufficiency (1) simple myohemoglobinuria without any sign of uremia, and with a favorable prognosis, (2) myohemoglobinuria with cyclic vomiting, restlessness, myocardial insufficiency, transitory anuria, albuminuria, hematuria, and cylindruria, (3) severe nephrosis with a very unfavorable prognosis (without the use of an artificial kidney, this form of the disease is fatal)

Acute Pancreatitis—Poilleux and Davy (*Ann Chir*, January, 1960) reported a series of 14 patients with acute pancreatitis, 5 of whom died In the first stage of the disease, operation should be avoided and emphasis should be given to combating shock The maintenance of electrolyte balance is indispensable The intravenous administration of 100 to 400 mg of hydrocortisone hemisuccinate per day gave good results Therapy with procaine was the best means of controlling pain In order to reduce the pancreatic secretion, strict fasting and continuous aspiration of the stomach was imperative A laparotomy during the phase of improvement permitted the exploration of the pancreas

Diabetes Insipidus—The differential diagnosis between diabetes insipidus ascribed to lack of antidiuretic hormone and the true polydipsias ascribed to potomania is difficult Two tests may be used The first is that of Cates and Garrod in which an injection of nicotine is given intravenously in an attempt to provoke an antidiuretic hormone secretion in a patient who, after the massive ingestion of water, has polyuria The second test, that of Carter and Robbins, tries to obtain the same results by the intravenous perfusion of hypertonic saline solution With any of these tests the provoked polyuria was reduced by 80% in patients with potomania and in normal persons, but this reaction did not occur in patients with diabetes insipidus

The second test is more specific, but it is complicated in that the intravenous perfusion requires 45 minutes and a catheter must be introduced into the bladder to measure the excreted urine every minute Its interpretation is also difficult A simple clinical test was reported on by J Decourt and co-workers at the meeting of the Medical Society of the Hospitals of Paris The patient to be examined is given nothing to drink after the evening meal taken on the eve of the test This should be done under close surveillance of the patient In the morning, the patient experiences an intense thirst At 8 a m the still-fasting patient urinates and is given 200 cc of water to drink at 8 00, 8 15, and 8 30 The voided urine is collected until 10 30 and its volume, sodium-chloride content, and density is measured On the next day the same test is carried out but at each ingestion of 200 cc of water the patient is given a tablet containing 1 8 Gm of sodium chloride

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The items in these letters are contributed by regular correspondents in the various foreign countries

During these two tests the patient remained in bed, and was weighed before and after the ingestion of water, and after micturition at 10 30 In case the patient defecated during the two tests the feces were also weighed In normal persons and in those with potomania, diuresis was inhibited by the ingestion of sodium chloride The reduction of diuresis was in proportion to the ingested dose of sodium chloride In patients with diabetes insipidus, however, this reaction did not occur, in some an increase in polyuria was observed This test, which is easy to perform, gives the same results as that of Carter and Robbins and may, therefore, replace it

Meprobamate in Pediatrics—R Didier (*Gazette médicale de France*, Jan 10, 1960) treated a series of 250 infants and children, ranging in age from several months to 15 years, for two years with meprobamate Improvement was noted in 25% of the children with speech disorders of the spastic type Behavior disturbances and psychoneurotic disorders associated with anxiety were favorably influenced by this drug The migraine syndrome was improved in the 67% of patients who had it The drug had a favorable effect on the neuropsychic element in those with asthma Improvement in spasmodic cough was also noted Such disorders of puberty as lipothymia, dizziness, tremor, and minor respiratory disturbances disappeared Improvements were observed in tachycardia, in such pains as seen in angina pectoris, and in palpitation This drug, however, had no effect on the vasomotor disturbances Treatment with meprobamate for long periods of time was well tolerated

GERMANY

Prednisone for Sarcoidosis—Schaper and Schnell (*Medizinische*, no 52, p 2575, 1959) stated that sarcoidosis is much more frequently encountered than it was thought to be in the past Although the cause of the disease is not definitely known, some observers believe it is related to tuberculosis Mycobacterium tuberculosis has been found in only a few patients with sarcoidosis Histological examinations have shown many parallels to tuberculosis, but central necrosis is always absent in sarcoidosis The most recent observations in tuberculous patients who had been treated with tuberculostatic drugs also suggested a connection between the two diseases In these patients, the type of giant cell associated with sarcoidosis has been found and central necrosis was absent It may be concluded that necrosis, when it occurs, is caused by live tubercle bacilli, although the epithelioid and giant cells are caused by the effect of the body's degradation products of these organisms on the mesenchyme

It appears that in sarcoidosis a natural excess of defensive powers causes the early destruction of the tubercle bacilli, while in the manifest infections the bacteria are killed only by the administration of tuberculostatic drugs When sarcoidosis is understood as an excessive mesenchymal reaction, corticoid treatment is indicated Marked improvement and even cure has been achieved The results of steroid treatment were most convincing in patients with pulmonary changes, but it is also indicated for patients in whom only the hilar lymph nodes are enlarged in order to prevent pulmonary dissemination The ocular changes that occurred in sarcoidosis also responded promptly to adrenocortical hormone therapy

Antibiotics for Hepatic Coma—G A Martini and co-workers (*Medizinische*, no 52, p 2549, 1959) stated that patients with cirrhosis are endangered by hepatic coma because of toxic substances formed by the action of bacteria on the nitrogen-containing intestinal content In most such patients, the blood ammonia level is raised and ammonia is absorbed from the intestine, which, via the collateral circulation, directly reaches the major circulation and cannot be detoxified in the liver The ammonia causes cerebral intoxication Hepatic coma is frequently initiated by bleeding from esophageal varices A new treatment of hepatic coma is based on the pathogenic hypotheses The patients are given a protein-poor diet and rapid evacuation of the intestine is promoted Antibiotics are given to destroy the intestinal bacteria

This treatment was used in a series of 30 patients with hepatic coma Patients who had bleeding from esophageal varices required blood substitution and hemostasis The results of treatment were markedly superior to those obtained in a group of patients in whom antibiotics were not given All patients who were treated with antibiotics survived the hepatic coma, although the treatment had no effect on the underlying condition Neomycin has now replaced the previously used tetracyclines, since these antibiotics are poorly absorbed from the intestine Since blood level determinations showed a neomycin content in 7 of 27 patients, this treatment too requires observation for side effects, especially on the eighth cranial nerve and the kidneys

A reduction of the ammonia content in the blood was seen in all patients Since varicose bleeding is often the precipitating cause of hepatic coma, neomycin should be given immediately when bleeding occurs in order to prevent hepatic coma Neomycin is also suitable for patients who are hypersensitive to protein and in whom the daily intake of 20 to 40 Gm of protein causes the blood ammonia level to increase These patients require treatment for several months

INDIA

Salmonella Paratyphi A—M W Kirtikar reported the results of bacteriophage typing of 371 strains of Salmonella paratyphi A Of these, 135 came from various cities in India and the rest came from Australia, Belgium, Canada, Czechoslovakia, Egypt, Germany, Hungary, Indonesia, Israel, Italy, Norway, Russia, United States, and Yugoslavia The strains that showed no reaction with the available typing phage preparations (6 14%) were termed untypable Of all the strains studied, 80 37% could be definitely typed, 5 07% were "degraded" strains, and the rest were as yet unclassified The commonest phage-type throughout the world was found to be type 1 except in Africa and especially Egypt where the commonest type isolated was type 4 (type 1 was second) Type 2 was next in order in all the other continents Type 3 came mostly from Europe and especially Italy and Hungary It was almost nonexistent in Africa, America, and Australia

Bacteriological Study of Resected Tuberculous Lungs—D Barua and co-workers (*Indian J M Res* 48 263 [May] 1960) studied 216 tuberculous lesions from pulmonary resections of 52 patients Acid-fast bacilli were demonstrated by smear examination in 84 6% of the specimens, by culture in 36 5%, and by guinea pig inoculation in 32 7% The results of cultural and animal inoculation tests were not always identical, 40 4% of the specimens yielded viable bacilli (32 7% were viable-virulent and 7 7% viable-avirulent) In 15 4% no acid-fast bacilli were found by any of the three methods The incidence of viable bacilli was significantly higher in circumscribed lesions containing liquefied material, 75% of such lesions contained viable bacilli while of the rest 48 5% of the cavernous lesions, 16 7% of the caseous lesions, 3 7% of the inspissated lesions, and only one of five calcified lesions showed viable bacilli

The viability of bacilli varied in the same specimen in different lesions Of the 50 strains isolated from different lesions, 48% were resistant to streptomycin, 46% to isoniazid, and 12% to PAS Strains from different lesions of the same patient showed the same sensitivity pattern Sensitivity was not related to the amount of drugs taken by the patient, probably because of the irregular treatment received Ten of the 50 viable strains were avirulent to guinea pigs They were resistant to isoniazid Patients who had received different combinations of drugs within less than a year showed a proportionately large number of nonviable bacilli, but histological evidence of continued activity even with nonviable or viable and avirulent bacilli was seen

The bacteriological findings could be correlated with the anatomical type of lesion to a certain extent, but not always with the total amount of drug administered and the duration of the disease The incidence of drug resistant strains as shown by this study was not high as compared to reports from other countries, 12% of strains that were resistant to PAS were also resistant to the other antituberculous drugs The sensitivity pattern was also unrelated to the duration of disease Most of the strains were catalase positive except those with a high degree of resistance to isoniazid The neutral red test was positive with all the organisms isolated including the 10 avirulent strains Production of catalase could be correlated better with the guinea pig inoculation test than with the neutral red test as seen by histological evidence of activity, but the authors believed that a positive neutral red test might be a better indication of virulence in spite of a negative animal inoculation test

Copper in the Liver—Balasubramanyan and Chopra (*Indian J M Sc* 14 351 [April] 1960) studied 210 specimens of liver obtained by needle biopsy for the presence of copper The specimens came from 29 normal controls and 181 patients with various diseases The sections from normal liver and those from the patients with carcinoma, leukemia, chronic passive congestion, and tuberculosis did not show any copper The 39 patients with anemia showed changes which could be attributed to mild protein deficiency but no copper Specimens from patients with fatty liver and infectious hepatitis, biliary cirrhosis, and obstructive jaundice also failed to show any copper

The one patient with hemachromatosis had an extensive deposition of copper Of the 59 adults with cirrhosis, 2 had small amounts of copper in the liver cells The 25 infants with cirrhosis were all between the ages of 1 and 3 years, and 19 gave a positive staining reaction for copper The authors stressed the finding of heavy deposits of copper in a large proportion of patients with infantile cirrhosis in contrast to the low incidence in adults with cirrhosis and suggested that infantile cirrhosis might be due to a metabolic disorder

Chronic Granulocytic Leukemia—Ghose and Chatterjea (*J Indian M A* 34 381 [May 16] 1960) found that chronic granulocytic leukemia was the commonest type of leukemia in Indians In a series of 116 patients with this disease, the maximum incidence was seen in the age group of 23 to 32 years The commonest mode of onset was with splenic enlargement, others had asthenia and fever as the main symptom at onset Early diagnosis even when followed by timely therapy did not necessarily prolong life The treatment consisted of ethyl carbamate, deep x-ray, and busulfan, singly or in combination Analysis of results showed that carbamate was definitely inferior to both busulfan and deep x ray while response to these two was similar Although the disease remains incurable, the authors found that with judicious application of radiotherapy and busulfan therapy or both, most patients show worthwhile remissions and are able to lead useful lives

Single Operation for Entropion with Trichiasis and Trachoma—L P Kapur (*Indian M J* 54 81 [April] 1960) described the technique of an operation for the treatment of advanced cases of entropion-trichiasis and trachoma when they are present together It consists essentially of removal of the tarsal plate from the lid, thus curing both the disabilities without interfering with the function of the lid and its glands except possibly a few meibomian glands The only drawback of the operation is that a papilla of the conjunctiva may appear in a few patients after the operation This can be snipped off after everting the lid Its appearance can be prevented, however, by clean and even suturing of the lid at the end of the operation The author found this operation safe There were no recurrences or apparent disfigurements, as the shortening of the lid, which may result, is negligible

Treatment of Leprosy—A T Roy (*Indian M J* 54 84 [April] 1960) gave SU-1906 a derivative of diphenyl thiourea that is active against tuberculosis, to seven patients who had leprosy, none of whom had had any previous antileprosy treatment These patients were observed for 21 months The maximum tolerated dose was found to be 4 5 Gm, beyond which toxic reactions appeared With the usual recommended dose of 1 to 3 Gm, none of the patients showed any toxic reactions Marked clinical improvement and rapid fall of bacillary index were noted after four months of treatment After 8 to 12 months, the bacillary index again rose, but after 12 to 16 months the progress was good with slight deterioration again after 17 to 21 months

The deterioration noted may have been due to use of the maximum tolerated dose early in the period of observation, and the deterioration later on may have been due to the onset of the hot season The hemoglobin level and total and differential blood counts were not altered by therapy with the drug The drug exhibited a definite antileprotic action and has the advantage that it can be used for all types of leprosy for prolonged periods

Tropical Eosinophilia—B S Kulkarni and coworkers (*J Postgraduate Medicine* 6 60 [April] 1960) studied the plasma protein patterns in patients with tropical eosinophilia with a view to determining whether changes in these are consistent with the present concept of the nature of this disease, viz, that the condition is due primarily to a parasite and such manifestations as eosinophilia and bronchial spasm are allergic responses to the continued presence of this parasite A series of 43 patients who had predominantly respiratory symptoms, an absolute eosinophil count of over 4,000 per cubic millimeter, and who showed a therapeutic response to arsenic or diethylcarbamazine were studied As compared to normal subjects from the same social strata and of the same mean age and dietary habits, a significant elevation was seen in the mean levels of total protein and alpha 1, alpha 2, and gamma globulins while the albumin fraction was significantly lowered The albumin/globulin ratio was reversed

No correlation was seen between changes in plasma proteins and the degree of eosinophilia The rise in gamma globulin was moderate and of the same extent as seen in such other chronic conditions as rheumatoid arthritis, periarteritis nodosa, and chronic pulmonary tuberculosis Lowering of the albumin level could be considered a nonspecific change as it occurred in almost every febrile illness Increase in the alpha 2 fraction was likely to be due to increase in glycoproteins which occurred in the acute or progressive stage of many infections and might be partly responsible for the increased sedimentation rate often associated with this disease

SWEDEN

Nuncital for Mental Ailments—Dr B Scherstén (*Svenska lak -sallsk forhandl* [April 14] 1960) treated 65 patients with 3-methyl-3-pentanol carbamate (Nuncital) Of these, 26 had psychogenic and psychosomatic ailments Since the sedative component of certain tranquilizers has been eliminated in this drug, it was effective as a muscle relaxer in patients with cardiovascular and gastrointestinal diseases In the same issue Dr S Martens related his experiences at the Alcohol Polyclinic in Stockholm where the reactions of 60 patients were studied The effects of the drug were compared with those of meprobamate and a placebo Both the carbamate and meprobamate were significantly superior to the placebo, and the carbamate was superior to meprobamate in alleviating nervous symptoms Its side-effects were less than were those of meprobamate During a long-term study of its toxicity in chronic schizophrenics, no changes attributable to the drug were found in the blood, urine, or liver

Complications of Chlorpromazine Treatment—After five years of experience with chlorpromazine at the Beckomberga Hospital, Jonsson and Ågren (*Nord med* [April 21] 1960) reported on a series of 4,500 patients, 67 per cent of them women, treated with this drug When this treatment was prolonged, the risk of hematological complications rose, and women appeared to be more susceptible to them than men Jaundice sometimes developed early during treatment and was independent of the dosage of the drug Such jaundice was benign and was independent of earlier ailments of the liver and not likely to inflict permanent damage Eosinophilia might be a precursor of jaundice, the onset of jaundice could not otherwise be anticipated After the age of 50, the risk of drug-induced blood diseases might increase After leukopenic and granulocytopenic changes in the blood occurred, further treatment with the drug required strict control and full appreciation of the attendant risks Severe conditions sometimes appeared without warning symptoms

Hydroxydione for Alcoholic Psychoses—At the Maria Clinic in Stockholm, Dr R Dimberg (*Svenska lak-sallsk forhandl* [April 8] 1960) gave hydroxydione to 101 men suffering from various forms of alcohol poisoning such as delirium tremens and hallucinations As many as 70 of them had previously been in some mental hospital The drug was given either by comparatively rapid intravenous injection of a 5 per cent aqueous solution or by intravenous infusion of a solution containing 6 per cent dextran or 5 per cent dextrose, the usual doses were 250 mg and 1 Gm respectively All of the 23 patients suffering from hallucinations were rid of them on the first day of treatment, and all the predelirious and delirious patients were free from symptoms within three days In only eight patients did the treatment have to be repeated during the acute phase The drug seemed to have a specific antidelirious effect, and its freedom from side-effects added to its usefulness The promptness with which it acted did much to facilitate the nursing of patients during the acute phases of their illness

UNITED KINGDOM

Chemotherapy of Smallpox—Smallpox still takes its toll of life, particularly in underdeveloped countries where vaccination is rarely practiced There are about 31,600 deaths in the world from this disease every year There is, thus, a definite need for a specific antiviral chemotherapeutic agent for its treatment Several years ago Bauer found that isatin β-thiosemicarbazone had a pronounced chemotherapeutic effect in mice infected intracerebrally with neurovaccinia virus and with rabbitpox Many derivatives of this compound were then prepared, and Bauer (*Lancet* 1 1110, 1960) reported that one of them, N-ethylisatin β-thiosemicarbazone, protected infant mice against the effects of 100 times the LD$_{50}$ of alastrim virus given intracerebrally The Schofield strain of alastrim virus was passaged on chorioallantoic membrane eight times and through the brains of infant mice three times It was then given intracerebrally to infant mice

Of the mice given N-ethylisatin β-thiosemicarbazone at the time the virus was injected, 91% survived without showing any sign of illness Of the control mice who had the same dose of virus but no chemotherapy, 75% died and 15% developed a nonfatal encephalitis The dose level that conferred 50% protection against infection was about 0 25 mg per kilogram The compound is of low toxicity, mice tolerating a dose of 500 mg per kilogram without signs of illness This gives a therapeutic index of over 2,000 An activity of this order is greater than that of the sulfonamides or tetracyclines With such a high activity and low toxicity Bauer believed that N-ethylisatin β-thiosemicarbazone should be of value in the treatment of smallpox in man

Glucagon for Hyperinsulinism—Glucagon, which, acting with insulin, probably facilitates glucose transport from the liver to peripheral tissues and its utilization there, causes a rapid rise in blood sugar level if injected into normal subjects The rise is maximal in 30 to 45 minutes, and the blood sugar level then returns to normal in about two hours Marks (*Brit M J* 1 1539, 1960) has examined the response to glucagon of subjects with hyperinsulinism due to islet cell tumors He observed that in hyperinsulinism the injection of 1 mg of glucagon intramuscularly was followed by a rapid rise in blood sugar level, and in a patient with symptomatic hypoglycemia it was accompanied by temporary clinical improvement, but after two hours severe hypoglycemia set in, necessitating termination of the test This effect was neutralized by administration of glucose Marks suggested that the response to glucagon might be used to distinguish patients with hyperinsulinism from normal subjects and in the differential diagnosis of the hypoglycemic syndrome

Kinked Innominate Vein Syndrome—A new syndrome has been described by Dr K Shirley Smith (*Brit Heart J* 22 110, 1960) who terms it the kinked innominate vein syndrome He showed that compression of the innominate vein by an enlarged and high aortic arch obstructs the venous flow in the chest, thereby causing distention without pulsation of the left deep jugular vein while the right pulsates freely in the normal manner In this condition the venous pressure in the left antecubital vein is higher than that in the right Thus, the demonstration of unilateral venous engorgement in the neck can be due to impaired venous inflow into the right side of the heart and is not necessarily associated with a cardiac abnormality

In the absence of a mediastinal mass the syndrome is diagnostic of a high and rigid aortic arch Smith believed that increased rigidity of the latter is probably responsible for the compression of the innominate vein, because it is not seen in patients with coarctation of the aorta, in which condition the high aortic arch pulsates freely If pulsation is easily felt in the suprasternal notch and if there is a kinked left innominate vein, a diagnosis of increased aortic rigidity is likely

Abdominal Decompression in Labor —The application of negative pressure to the abdomen during the uterine contractions of the first stage of labor was first described last year by Prof O S Heyns of Johannesburg He conceived the idea that if the abdominal wall were drawn forward by negative pressure the uterus would become spherical during a contraction instead of being deformed into an ovoid When spherical the uterus is in its optimal position for contraction Scott and Loudon (*Lancet* 1 1181, 1960) have developed an apparatus on the principle described by Heyns The three main components are an apparatus for producing suction, a plastic suit to cover the abdomen, thighs, and lower part of the chest, and a wire cage to support the suit The suction apparatus withdraws air at the rate of 50 liters a minute from the plastic suit, which is made of 200-gauge polyethylene and fits over the body from the level of the axilla to the top of the thigh The wire cage made of flexible steel rods, maintains an air space between the plastic suit and the abdomen Without it, the suit would collapse on to the skin, and the abdominal wall would not move The plastic suit costs only 28 cents and can be discarded after use

Decompression is commenced when uterine contractions become painful and a sedative would normally be given The membranes are then ruptured and the patient fitted into the suit On evacuating air from it the abdomen rises forward The suction is applied continuously, and the patient controls the pressure herself at between -20 and -40 mm Hg by occluding with her thumb a rubber tube leading from the interior of the suit Negative pressure is applied only for the duration of a pain The fetal heart sounds can be recorded by an electronic monitoring device to avoid undoing the suit Although patients in the supine position can be managed, sitting in a chair is a better position for them It is too early to assess the results of this new technique, but Scott and Loudon claim that it reduces the pain and duration of the first stage of labor The relief of pain is convincingly demonstrated by the reluctance of the patient to have the suit removed for pelvic examination, the frequent finding of full dilatation of the cervix in primigravidae in under three hours of the commencement of distressing labor pains is evidence that decompression profoundly alters uterine action Internal tocography shows that uterine contractions are of normal duration

Griseofulvin —Brian Russell and co-workers (*Lancet* 1 1141, 1960) measured the effects of prolonged treatment with griseofulvin by comparing a group of patients treated with it with a control group given inert tablets No local treatment was used To limit the trial to the minimum number of patients it was planned on a sequential analysis basis The dose was 1 5 Gm daily by mouth The results were stated to be so striking that even without controls there was no doubt of its value

In the first trial a group of patients treated with griseofulvin for four months was compared with a group given a placebo for the same period Thirty-one of 33 in the treated group and only 1 of 31 controls showed definite clinical improvement Side-effects were the same in both groups Treatment of the 33 patients initially given griseofulvin was continued for periods ranging from 4 to 12 months, and 11 more patients were followed up for a year Clinical improvement was noted in most instances within two months Appearances were usually normal by four months, and all the skin lesions had cleared by the ninth month Most patients with fingernail lesions improved after three months' treatment, but only 62% of those with toenail lesions improved in this time By the 10th month 80% of those with fingernail lesions had normal nails, compared with 12% of those with toenail lesions Even after a year only 20% of the latter had become normal Skin lesions cleared more rapidly, 40% becoming mycologically negative within two months, although only 22% with toe-web infections were negative within this time After 2 to 10 months of treatment 13% of patients with skin lesions still remained positive, compared with 70% of those with affected fingernails and 85% with affected toenails All the fingernail infections, but only 25% of those of the toenails, were negative after a year

A diminution in the immediate positive reaction to the trichophytin test was observed during treatment in a limited number of patients No undesirable effects were observed It was concluded that griseofulvin is a safe, effective remedy for chronic ringworm infections, although long-term treatment is necessary The failure of treatment in many toenail infections was attributed to the slow outgrowth of toenails The problem with most ringworm infections is recurrence which is due to reinfection

CORRESPONDENCE

RELATIONSHIP OF MEDICINE WITH ALLIED HEALTH PROFESSIONS

To the Editor —Wisely the American Medical Association is undertaking a systematic study of its relationships with allied health professions and services An impressive committee is arranging for a series of conversations with officials of various organizations associated in the general health effort These organizations include scientific groups representing experimental biology and the basic sciences for the health professions as well as various allied health professions The number of these organizations is growing They illustrate clearly the tremendous expansion of health services and activity

The A M A Committee to Study the Relationship of Medicine with Allied Health Professions and Services is composed of members of the Board of Trustees, and representatives from the Council of Medical Education and Hospitals and the Council on Mental Health Dr Raymond M McKeown is chairman, and Dr John Hinman is secretary The proceedings of the 1959 conferences have been issued in mimeographed form totalling 256 pages A mere listing of the groups involved in the conversations would clearly indicate to practicing physicians the extraordinary expansion of health activities It is heartening that the A M A is taking the leadership in promoting mutually respectful and mutually cooperative relationships between the various health professions and services so that ultimately the goal of promoting optimum health for all our people can be approached

This implies a significant shift of emphasis While medicine as a profession has been concerned for centuries with the management of disease when it comes along, it has now been possible to turn attention toward the more pertinent problem of preventing disease With the success of preventive medicine and the public health effort, it is now possible to begin thinking in even more positive terms of developing a broad program for promoting the optimum health of the people

This brings a real challenge to all the allied health professions and services The challenge in part deals with ways and means whereby individual members of the allied health professions and services can obtain their livelihood in an economically free society on the basis of promoting optimum health This challenge will require careful consultation with representative public leaders, such as economists, lawyers, sociologists, and political scientists, for the purpose of devising procedures whereby members of the allied health professions and services can earn a decent living on the basis of promoting optimum health for individual clients and in caring for illness or injury if such occurs Here is a chance for the exercise of professional responsibility in a free economy If the opportunity is lost, then there is increasing likelihood for increasing social organization of the health professions and services, which would be unfortunate It is much more desirable all around in a democracy such as that in the United States that governmental regulation be reduced to a minimum Such regulation can only be prevented if conscientious citizens will assume the responsibility for voluntary association and regulation directed toward the accomplishment of a common purpose If the allied health professions and services can agree on the promotion of optimum health as a worthy common objective and devise an appropriate economic pattern to support it, there will be lasting benefit to the American people

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METHAMINODIAZOPOXIDE

To the Editor —In reference to the article by Harris, "Methaminodiazopoxide," in The Journal, March 12, page 1162, I wish to report the incidents of unpredicted side-effects in a study carried out on 68 drivers taking methaminodiazopoxide (Librium) in adjusted maintenance doses ranging from 10 to 100 mg daily In a 90-day period, 10 minor and 6 major road accidents occurred in this group, a tenfold increase on projected statistics provided by the highway department These accidents were not primarily due to spinocerebellar dysfunction but appeared to be evidence of change in driving habits resulting from psychological effects of this substance in liberating aggressive, euphoric, or underlying self-destructive tendencies

In addition numerous falls, dropping of objects, and laceration of hands with sharp objects were reported in this study of 116 patients Three falls caused fracture of bony structure one broken femur in a woman aged 51 years, a fractured external malleolus in a woman aged 49 years, and a broken fibula in a man aged 35 years Sudden directional changes involving body-righting mechanism disorganization preceded these falls Ataxia was a cumulative phenomenon, to be detected by the following test The patient was asked to stand erect, keep his eyes closed throughout the test, face forward with his arms outstretched, nod his head in a gesture of affirmation, and come to rest in an erect position Next he was asked to nod his head in a gesture of negation and come to rest face forward Dysequilibrium at any stage may be classified as modified Romberg 1, 2, or 3+ Ataxia was characteristically present without subjective awareness These findings would detract from the statement that methaminodiazopoxide would appear to have a margin of safety greater than meprobamate The suggested site of action of the substance is in the limbic system and septal brain area It acts as a stimulant with 'anti-repressant" characteristics, which explains the paradoxical reactions If homeostasis is to be preserved, psychological defense mechanism changes brought about by the substance require close psychotherapeutic supervision

It is strongly recommended that more detailed pharmacological studies be carried out with this substance before its general and non-specific administration is begun Changes in driving behavior in these patients occurred insidiously and cumulatively becoming manifest usually after they had been taking the substance for about four to six weeks Patients taking this substance should be warned against the dangers of possible changes in driving habits since the potential liberation of latent hostile, self-destructive, or impulsive behavior patterns compounded by spinocerebellar disturbances might impair their safety and judgment so that they may become a danger to themselves or to other innocent persons

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PRESIDENT W H HARRISON DID NOT PRACTICE MEDICINE

To the Editor —In The Journal, May 21, page 296, it is stated, "No president of the United States has had a medical background" May I suggest that staff of The Journal do a bit of research on the background of William Henry Harrison (1773 to 1841), ninth president of the United States I believe they will find that President Harrison practiced medicine for a short while I have forgotten the facts relative to his activities as a medical man, although I believe he acted as a combination line officer and medical officer in the Indian Wars in Indiana

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The bit of research suggested by Dr Garceau led us through several books and encyclopedias before it was possible to say whether or not President William Henry Harrison ever practiced medicine Goebel's biography of Harrison (Indiana Historical collections, vol 14, Historical Bureau of the Indiana Library and Historical Department, 1926) answers the question in the negative It appears that Harrison attended Hampden-Sidney College for a time, the extent of which it is impossible to determine, and then attended an academy in Southampton for a short time before going, in 1790, to Richmond, Va, where he took up the study of medicine at the age of 17 under a Dr Leiper Within a few months, however, he decided to go to Pennsylvania and continue his studies under Dr Benjamin Rush and Dr William Shippen, then president of the College of Physicians in the University of Pennsylvania In 1791 Harrison decided that he disliked medicine and wanted a career in the Army So, through the influence of Governor Richard Henry Lee, who was visiting in Philadelphia at the time, Harrison obtained a commission as "ensign" in the First Regiment of the U S Infantry and thus began a military and political career that eventually led to the White House —Ed

TREATMENT OF INFECTIOUS MONONUCLEOSIS

To the Editor —The Journal occupies a very unique place in American medicine While its responsibilities are many, one of the most important would appear to be the field of applied therapeutics, a subject of the greatest concern for the practicing physician Therefore, papers which deal with treatment should receive the closest scrutiny prior to publication, not only because they can be misleading to the physician but also because they can exert a deleterious effect upon the relation between doctor and producer A case in point is a recent publication (Gothberg, L A Severe Infectious Mononucleosis Treated with Chloroquine Phosphate, *J A M A* 173 53 [May 7] 1960) in which it is "demonstrated" that chloroquine is an effective drug for the treatment of infectious mononucleosis The physician reading this report might conclude that such is the case The astute detail man might, with some propriety, do likewise and subsequently present his product in a favorable light for the management of this disease In truth, the paper demonstrates nothing of the sort It deals with only four patients, each treated for a rather lengthy period Each patient already had a positive heterophil antibody test at the time that treatment was begun, in no instance was there evidence that the basic hematologic abnormalities had been reversed by the drug More seriously, no information is given as to the number of similar patients, if any, who failed to respond to the same treatment schedule There may be occasions when early and, perhaps, premature reports of therapeutic measures should be presented to the profession, but I believe that this would be proper only for diseases that are so rare as to preclude any one investigator's acquiring a sufficient number of cases except over a period of years

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The communication by Gothberg was published in the special section, Preliminary Communication It was accepted as a preliminary report, and no attempt was made to disguise this feature —Ed

PNEUMONITIS DUE TO CHEMICAL IRRITANTS

To the Editor —Since the introduction of the anti-inflammatory steroids there have been sporadic reports of their use in patients with pulmonary edema arising from the inhalation of chemical irritants (Prosad, B N *Arch internat pharmacodyn* [pt 2] 114 146 [March 1] 1958) These reports suggest that the steroids are useful and even life-saving in patients who have inhaled chlorine (Holmes, G Personal communication to the author), oxides of nitrogen (Lachnit, von V *Zentralb Arbeitsmed u Arbeitsschutz* 8 177 [Aug] 1958), crude oil (Graham, J R *Tr Am Clin & Climatol A* 67 104, 1955), and stomach contents (Marshall, B M, and Gordon, R A *Canad Anaesth Soc J* 5·438 [Oct] 1958), but because of the small number of cases, it is not yet possible to recommend steroid therapy as a routine form of therapy for such patients In order to correctly evaluate this method of treatment, it is necessary to assemble more cases Therefore, I should be grateful if any readers of The Journal who have used steroids in treating pneumonitis arising from chemical irritants would write to me outlining their experience, whether it was favorable or unfavorable It is not suggested that other well-established forms of therapy, such as antibiotics and oxygen, should be abandoned but rather that in certain circumstances steroids might be added to these measures

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REFERENCE TO BERRY

To the Editor —You are running some beautiful sleepers, but some of them are a little confusing You have a fine editorial on "Theodoric on Surgery" in The Journal, May 14, page 176 This is a delightful editorial Then you bring in on the last paragraph a reference to Berry You have not said a thing about him in the whole editorial, and he all of a sudden pops up with sort of a bang Is it your idea that we had better go back and see who Berry is? This is all right, but it may upset some of your readers

Certainly you can be proud of the fine way in which the whole program of The Journal is rolling along I am glad that the correspondence column is attracting interest Keep happy and enjoy yourself

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GENERALS WOOD AND PERSHING

To the Editor —Dr James A Tobey, in "The Physician Who Was Nominated for President," in The Journal, May 21, page 296, omitted one unusual feature in his biography of Leonard Wood In 1923 General Wood was appointed provost of the University of Pennsylvania, a post he held for one year, although he never appeared on or near the campus for one second during that time Dr Tobey evinces some surprise that "Black Jack" Pershing was promoted from captain to brigadier general over the heads of 862 officers who outranked him It was perfectly simple Captain Pershing had married the daughter of Senator Warren, who was the chairman of the Senate Armed Forces Committee

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FINGERNAIL GRAFTING

To the Editor —In The Journal, Feb 27, page 990, there was an inquiry regarding the possibility of grafting a fingernail This called to mind a patient seen in the skin clinic at Northwestern University Medical School years ago The woman had had a defect at the end of her nasal septum repaired by a graft from the tip of a finger When this tissue was taken for grafting, a part of her nail fold had been included, and when I saw her there was a small fragment of fingernail growing on the lower nasal septum This is an example of an unintentionally successful graft

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BOARD EXAMINATIONS

To the Editor —Your editorial, "Acceptance of Responsibility," in The Journal, May 14, page 177, is timely I notice a lack of emphasis on the use of methods and procedures at board examinations, which as a rule stress academic or "ivory tower" knowledge and fail to evaluate the candidates' knowledge and ability to face and act in the practical world of everyday medicine in the United States

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BOOK REVIEWS

Medical Care of the Adolescent A Textbook Concerning the Medical Care and Understanding of Adolescents Themselves and of Their Disorders By J Roswell Gallagher M D Chief of Adolescent Unit, Children s Hospital Medical *Center, Boston, and staff physicians of Adolescent Unit Cloth* $10 Pp 369, with 43 illustrations Appleton-Century-Crofts, Inc , 35 W 32nd St , New York 1, 1960

The stated purpose of this book is, 'to discuss those ailments which are common in adolescence or which present some peculiarity during that period of life" and 'to emphasize the importance of taking adolescents themselves, their characteristics, their hopes and fears into account, and of treating them not just their illnesses " The format is excellent and conducive to pleasant reading References are given at the conclusion of each chapter The index is complete The length of the book is, if anything, inadequate for the material covered

The first four chapters, dealing with the general means and methods of evaluating the adolescent should be invaluable to one inexperienced with this age group These contain helpful points for those with wide experience The remaining chapters dealing with specific ailments, with several notable exceptions, suffer somewhat by the limitations of space The effort to be brief and concise has resulted in a degree of authoritative oversimplification The five chapters on gynecological problems and the one chapter on specific language disability are excellent The management of these *problems in this age group is difficult for many* physicians, and all should benefit from a careful reading of these chapters The presentations are excellent, and the significance of adequate management of these problems, in terms of the future well being of the individual, is probably much greater than one would suppose The two chapters on cardiovascular disease contain many useful points not available in other textbooks

Whereas the limitations of space have curtailed the discussion of various ailments, the treatment of the adolescent with an ailment has been excellently handled throughout The significance of any particular ailment to the adolescent has been emphasized, and many helpful thoughts are presented The importance of the physician adolescent relationship is emphasized, and many techniques to facilitate this relationship are presented The only defect is the lack of a discussion of the management of an adolescent with a fatal or potentially fatal disease Any physician dealing with adolescents should profit from reading this book It should be read by all medical students This book bridges the gap between the pediatrician s and of how to deal with a patient are not presented as such in the usual pediatric or medical textbook, and it is this approach that makes the book so valuable I fear, however, that many will not take the time necessary to carry out the precepts presented

William P Barba, II, M D

A Textbook of Gynecology By Lamar A Gray M D F A C S , F A C O G Associate Professor of Obstetrics and Gynecology, University of Louisville Medical School, Louisville Ky Cloth $15 50 Pp 470, with 324 illustrations Charles C Thomas, Publisher 301-327 E Lawrence Ave , Springfield, Ill , Blackwell Scientific Publications, Ltd , 24-25 Broad St Oxford, England, Ryerson Press, 299 Queen St , W , Toronto 2B Canada, 1960

This new textbook printed on good quality paper with good type is pleasantly readable The author has made some new approaches to facilitate the teaching of gynecology The purpose of the book is to present a new and modern summary of present-day gynecology in a brief and clear manner Most textbooks are much too detailed and contain so much philosophy that they are too voluminous for practical purposes This book may act as an outline for teachers, and, in addition, it is intended to interest the practicing physician

Pathology is stressed After the pathogenesis of the individual disease has been considered, the symptoms of the patient become more understandable Similarly, the diagnosis based on the physical examination and laboratory findings may be reached more logically, and the treatment can be more appropriately prescribed Certain operative techniques are described briefly The author spends much time describing the various hormones and their application to modern gynecology The effects of the emotions and personality factors in women have been recognized to be of tremendous importance in genital functions and must be reckoned with in the understanding and treatment of genital disease The illustrations are uncommonly effective

At the end of each section of the book are listed a few choice references Usually there are one or two historical references, one or two experimental papers, and, finally, two or three modern clinical articles which may introduce the student to the literature on gynecology The author starts out with a chapter, Patient Presents Herself,' giving history, examination, clinical impression, and disposition He follows this with a discussion of the various hormones and their application to modern gynecology Diseases of the vulva are described next, then diseases of the vagina and female urethra Other chapters describe the uterine cervix, including the modern concept of malignancies and unusual diseases, endometrium, menstrual functions and dysfunctions, and neoplasms, diseases of the myometrium, and the fallopian tubes Diseases of the ovary are well covered with discussion of the various types of tumor observed Endometriosis is covered in a separate chapter, followed by chapters on relaxations, displacements, and fistulas, diseases of the placenta and early pregnancy, hermaphroditism and congenital abnormalities, sterility, and menopause and its treatment

This well-written text is easily understandable, carefully prepared, it should be a valuable addition to anyone's library

BYFORD HESKETT, M D

The Pharmacopeia of the United States of America (The United States Pharmacopeia) Sixteenth revision, U S P XVI, by authority of The United States Pharmacopeial Convention, Inc, meeting at Washington, D C, May 9 and 10, 1950 Prepared by Committee of Revision and published by Board of Trustees Official from October 1, 1960 Cloth $10, $10 50 outside U S A Pp 1148 Mack Publishing Company, Easton, Pa, 1960

The 16th Revision of the Pharmacopeia of the United States of America has taken significant steps toward making this publication fulfill its objectives as a compendium of legal standards for the purity and potency of drugs which are included The prime criterion for inclusion is that a drug be a medicinal substance, the utility of which is fully established and well understood In this connection, it is important to note that the inclusion of patent drugs, begun with the 12th revision, has been greatly extended in the present edition A study of the interim admissions, the totally new admissions to this edition, and the deletions from the previous revision indicates the intensive efforts of the Committee of Revision in attempting to make this publication adequately represent current medicinal practice

The individual carefully prepared monographs incorporate new analytical techniques and indicate the care taken to eliminate ambiguities in test procedures

At the time of the first pharmacopeial convention, it was visualized that the Pharmacopeia would be of primary usefulness to physicians and apothecaries The legislative recognition accorded the Pharmacopeia has had a direct influence not only on its content but also on the area of its usefulness One indication of this is evidenced by the listing of over 50 drugs adopted for admission to the Pharmacopeia (some as far back as five years ago) but not yet included for lack of suitable analytical methods A further limitation recognized by the Committee is the inability to include all drugs of therapeutic merit due to time required for the operation of the process of selection A degree of compensation is provided by the knowledge that all drugs that are included have been judged to have therapeutic merit, a fact which gives the Pharmacopeia a relatively unique position among current therapeutic publications The course of the development of the Pharmacopeia as an official compendium is consequently associated with a decline of its usefulness to physicians and pharmacists Thus, the nature of the Pharmacopeia is such that it is of primary interest to drug manufacturers and federal and local drug enforcement officials

JOSEPH B JEROME, Ph D

Bentley and Driver's Textbook of Pharmaceutical Chemistry By J E Driver, Professor of Chemistry in University of Hong Kong, Hong Kong Seventh edition Cloth $14 50, 63 shillings Pp 728, with illustrations Oxford University Press, Amen House, Warwick Sq, London, E C 4, England, 417 Fifth Ave, New York 16, Amen House, 480 University Ave, Toronto 2, Canada, 1960

This latest revision of a standard textbook of pharmaceutical chemistry, having a record of extensive use in England and parts of the Commonwealth, was necessitated by the 1958 revision of the British Pharmacopeia It is an impressive work The material is divided into three parts Part 1 deals with physical and chemical methods used in determining the purity of pharmaceutical substances, part 2, with inorganic pharmaceuticals, and part 3, with organic pharmaceuticals

The book attempts to be inclusive and features condensed presentations of analytical methods used in the British Pharmacopeia as well as of such varied concepts as nuclear structure and reactions, atomic structure and types of chemical bonds, molecular weight determinations, and optical isomerism In spite of the inclusion of some relatively simple and basic chemistry, this does not appear to be a suitable text for instruction in pharmaceutical chemistry for students who are not already well grounded in inorganic and organic chemistry

In the sections on inorganic material, we find the chemistry of various elements briefly discussed in the familiar chemical groupings, followed by descriptions of official (BP) drugs containing these specific elements with a discussion of the applicable pharmacopeial tests In the organic pharmaceutical section, the usual classification system of organic chemistry is used, with brief discussions of individual drugs under the appropriate section The treatment accorded these compounds is adequate for the purpose intended, but it is difficult to understand the need for some of the more elementary sections on chemistry for persons judged capable of handling the chemistry of the more complex drugs

This book seems to be of more use as a source of review material for those studying for examinations in pharmaceutical chemistry (as the preface points out) or as a reference text for practicing pharmacists who wish to review the more recent developments in pharmaceutical chemistry The limitation of content material to drugs included in the British Pharmacopeia limits the area of usefulness of this textbook to England and the Commonwealth in spite of the expressed hopes of the publishers that it would prove of interest to a wider audience

JOSEPH B JEROME Ph D

The Story of Chemical Industry in Basle Published by Ciba Limited on occasion of its 75th anniversary Boards Pp 233, with illustrations Urs Graf Publishers Olten and Lausanne, Switzerland, 1959

This book is a history of the development of the Swiss organic chemical industry The genealogy and shape of the Basle chemical industry is portrayed from the preindustrial period in the late Middle Ages to the present The personal and contractual associations which characterized the early operations of CIBA Lt, Sandoz Ltd, J R Geigy S A, Durand & Huguenin Ltd, and Hoffman-La Roche & Co, Ltd, are briefly surveyed The growth of the several firms is related to the development of the dyestuffs, pharmaceuticals, plastics, textile products, and insecticides on which the chemical industry of Basle is based

The book is amply illustrated with drawings, woodcuts, and paintings depicting the historical setting of the late Middle Ages and Renaissance periods which preceded Basle s passage to the age of technology The culture and development of chemistry in Basle in the late 19th Century is also richly and extensively documented The acquisition of scientific knowledge and its technical utilization in the development of the five groups of chemicals for which the Swiss chemical industry is noted forms the main portion of this book It should be welcomed as a valuable contribution to the history of chemistry, particularly the origin of medicinal chemistry in Switzerland

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Hearing and Deafness Edited by Hallowell Davis M D Co-editor for revised edition S Richard Silverman Ph D Holt Rinehart book [Second edition] Cloth $7 95 Pp 573 with illustrations Holt, Rinehart & Winston, Inc 232 Madison Ave , New York 16, 1960

This text, at its first appearance over 11 years ago, was addressed to the intelligent layman interested in his own disability or that of others It was, however, more than a mere layman s guide In its present revised form, it has assumed an increased excellence and authority By adequate discussions, its 15 contributors have succeeded in making this text into an important aid, especially for the otologist and audiologist in training They have also provided a badly needed guide for physicians, psychologists, teachers of the deaf, and social workers as well as laymen

SAMUEL PEARLMAN M D

Edema Mechanisms and Management A Hahnemann Symposium on Salt and Water Retention Edited by John H Moyer, M D Professor and Chairman of Department of Medicine, Hahnemann Medical College and Hospital, Philadelphia and Morton Fuchs, M D, Assistant Professor of Medicine, Hahnemann Medical College and Hospital Cloth $15 Pp 833, with illustrations W B Saunders Company, 218 W Washington Sq , Philadelphia 5, 7 Grape St , Shaftesbury Ave , London, W C 2, England, 1960

This symposium is a comprehensive review of the mechanisms and management of edema by over 100 investigators and clinicians Since edema is not a problem peculiar to any one specialty in medicine, the authors comprise internists, pediatricians, surgeons, obstetricians, pharmacologists, physiologists, and biochemists

The symposium is composed of three main parts The initial chapters deal with the basic physiology of fluid and electrolyte balance as it pertains to the mechanisms of edema The complex interrelationships of the kidneys, adrenals, liver, lymphatics, and the cardiovascular system are discussed at length This is followed by several chapters on the pharmacological and clinical applications of the diuretic agents The mechanisms, uses, and efficacy of the xanthine diuretics, mercurial diuretics, triazine compounds, and the carbonic anhydrase inhibitors are discussed Considerable attention is centered on the thiazide derivatives The diuretic effects of the digitalis glycosides and adrenal steroids are mentioned as well as the new antialdosterone compounds (spirolactones) The remainder of the symposium deals with the clinical syndromes and pathological conditions associated with edema The mechanisms and therapy of edema due to renal pathology, liver disease, hypertension, congestive heart failure, toxemia of pregnancy, premenstrual tension, aldosteronism, and iatrogenic reasons are thoroughly discussed

The book is well illustrated with photographs, diagrams, charts, and graphs Each section is followed by a bibliography Because of its comprehensive approach to the broad subject of edema, this symposium should be available in all medical libraries It should be of value to any physician who encounters diagnostic and therapeutic problems involving edema

RODERICK DARBY

QUESTIONS AND ANSWERS

FETISHISM

To the Editor —*An adopted boy has shown abnormal behavior His twin sister is normal physically and mentally When he was 4 years of age, the foster mother first noticed that the boy would put on her stockings and then masturbate Merely looking at a picture of women's stockings would cause him to masturbate He is now 14, and his mother states that, if all women's stockings in the home are not locked up, he will put them on in private and then presumably masturbate If left alone in the home, he goes through drawer after drawer seeking women's stockings Stockings have been found hidden in his pillow case He usually denies his behavior but, when forced to admit it, says he cannot help it His mother and father are loving, intelligent parents This boy is quiet, co-operative, and not particularly introverted He plays baseball and other games with his classmates and gets average grades in school He and his sister were adopted 14 years ago by a married couple who were childless at the time, but who, three years after the adoption, became fecund and in the following six years produced five normal children of both sexes What can be done for this boy's behavior problem?*

Raymond A Abend, M D, East Syracuse N Y

Answer —This boy is suffering from the sexual perversion of fetishism, the compulsive associated use of an inanimate object to attain sexual gratification Other objects commonly used similarly are shoes, locks of hair, underclothes, and furs Such fetishism is rare in females The condition is not organic or hereditary but developmentally acquired, and it cannot be associated with the adoption in any way Since it is unconsciously compulsive and involuntary, the fact that the boy lies about it is not unusual, because parental prohibitions undoubtedly place him in a difficult, perhaps impossible, conflict situation

The superficial explanation for the condition is that it is determined by an accidental childhood experience associated with sexual excitement, which establishes a sort of conditioned reflex, but psychoanalytic studies have shown more positive meaning in terms of anxiety, particularly about castration or loss of the penis It represents a denial of the fantastic childish fear of the penisless state of the female This fallacious idea is not uncommon in young children Most children overcome it in the course of development The fetish-object is a sort of affirmation that the female too has a penis and a reassurance to the boy that his penis will not be lost

The boy should be seen by a psychiatrist for diagnosis and psychotherapy No drug or endocrine therapy is indicated It is unlikely that he would outgrow the condition or that it would improve simply through parental advice or forceful prohibitions

PERSISTENT COUGH

To the Editor —*In July, 1959, a woman who has paralysis agitans fell at home, fracturing her clavicle, and shortly thereafter developed an acute high blood sugar level (controlled), then aspiration pneumonia, urinary infection (controlled), and almost complete cardiac failure necessitating tracheotomy The tube was removed 30 days later She returned home early in October Her urine is normal, her lungs are in good condition, and with daily nursing there is much improvement in the spasticity She is able to walk with assistance The problem now is the persistence of a distressing harsh cough Could this be due to the cicatrix in the lumen of the trachea? If something can be found to minimize the cough I would be grateful The usual cough mixtures, both antihistaminic and sedative, do not help*

Percy O Chaudron M D, Cedartown, Ga

Answer —Cough after the removal of a tracheotomy tube is seldom due to a cicatrix in the trachea On rare occasions, a granuloma at the site of the tracheal stoma may interfere with the airway and, thereby, produce cough, however, this is unusual in adults and would not be expected in a patient in whom a tracheotomy tube has been used only 30 days Some of the factors which necessitated the tracheotomy may have recurred since decannulation With the muscular impairment which is present in patients with paralysis agitans, aspiration may again be occurring This could easily be a cause of the persistent cough Circulatory impairment with pulmonary congestion can also produce cough by its effect on the lungs or by irritation of the recurrent laryngeal nerve from enlargement of the left auricle

Unless the cause of this cough can be ascertained, improvement is not likely to be achieved, because symptomatic measures have already failed If aspiration is the cause of the persisting bronchial irritation, reestablishment of the tracheotomy

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The answers here published have been prepared by competent authorities They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply Anonymous communications cannot be answered Every letter must contain the writer's name and address but these will be omitted on request would provide the best means of maintaining proper tracheobronchial toilet The measures most likely to aid in determining the cause of the cough are careful evaluation of the cardiovascular situation, including fluoroscopic examination of the swallowing function, and bronchoscopy

MYALGIA

To the Editor —*A 30-year-old man gets a headache whenever the weather is cool or the wind is blowing, if he is not wearing a hat The headache is generally frontal, but not always It varies in character from dull to throbbing Antihistaminics or aspirin, or both, will abort it if taken early What treatment is recommended?*

M D , North Carolina

Answer —The patient appears to have myalgia or intrinsic allergy of the head Administration of a vasodilating agent on several successive days has helped some of these patients Nicotinic acid may be given orally in flushing doses two or three times daily, or histamine may be given intravenously in a dilution of 1 500,000 for 60 to 90 minutes

VENA CAVAL OBSTRUCTION

To the Editor —*A 40-year-old woman has a history of dizziness and swelling of two months' duration The mild edema has been confined to the breasts, abdomen, arms, and periorbital area This has been associated with a weight gain of 6 to 8 lb (2 7 to 3 6 kg) and dizzy spells Physical examination was unrevealing, with the exception of a palpable liver and some slight tenderness of the left lower abdominal quadrant The edema was of the nonpitting variety The patient has had some burning of her eyes, and a stinging sensation in the palms of her hands Her blood pressure was 125/70 mm Hg Results of complete blood count and urinalysis were negative She was given 0 5 Gm of chlorothiazide daily, which caused a remission of her symptoms, however, as soon as she discontinued the medication the edema returned Recently she has had no dizziness She was seen by an internist, who agreed that angioneurotic edema was a possibility but was curious about why the edema was so confined I am interested in other diagnostic possibilities and further tests to determine the cause of this edema*

George R Farrell, M D , San Diego, Calif

Answer —The data presented would appear to eliminate from consideration most of the usual causes of generalized edema, including those due to cardiac failure, the nephrotic state, hypoalbuminemia, or hypothyroidism Since the patient's swelling involves the part of the body in which the venous return is through the superior vena cava, obstruction of that channel causing the superior vena caval syndrome must be strongly considered In this syndrome, venous pressure elevation ordinarily is apparent clinically, with distended veins in the arms, neck, and scalp The presence of prominent superficial veins overlying the chest is also noted if the situation is chronic Measurements should be made of venous pressure in both upper and lower extremities, and if this measurement is definitely elevated in the upper extremities, further investigation should be made to determine the presence or absence of a vascular or neoplastic lesion causing superior venal caval obstruction

INFECTIOUS MONONUCLEOSIS

To the Editor —*What is the mechanism of the profound and prolonged asthenia that follows infectious mononucleosis? It is easy to understand this asthenia occurring after disease in which organ systems are involved, but, in infectious mononucleosis only the spleen and lymphatics are involved There does not appear to be any psychogenic factor in these cases, since these patients are usually in their late teens and have almost always been extremely active How is this post-infectious asthenia best treated? Are there any long-term sequelae in these cases?*

M D , New Jersey

Answer —Infectious mononucleosis is a generalized disease which may involve not only the spleen and lymphatics but any system Infiltration of the liver, as proved by hepatic biopsies, may be reflected by abnormal liver function tests in many patients without the symptoms of hepatic involvement Infiltrative pneumonitis is occasionally seen Convulsive seizures due to irritations of the cerebral cortex by excessive infiltration of lymphocytes are not rare If the diagnosis has been firmly established, the post-infective asthenia is best treated by watchful waiting and patience I know of no long-term sequelae

Answer —Infectious mononucleosis is a generalized systemic disease in which the liver is involved in a large percentage of, if not all, patients Hepatic dysfunction can be readily demonstrated, and alterations of the excretion of intravenously administered sulfobromophthalein, as well as increases in the serum transaminase level, are among the common abnormalities Jaundice appears in a variable but small percentage of patients The asthenia following infectious mononucleosis is not unlike that following viral hepatitis, and it may rightfully be assumed that it is due to the hepatic involvement As long as there is any evidence of hepatic involvement, it is appropriate to treat the asthenia after infectious mononucleosis as one would treat patients with infectious hepatitis, i e , with careful attention to rest and avoidance of excessive fatigue

HERPES ZOSTER AND LEUKEMIA

To the Editor —*I have a patient with chronic lymphocytic leukemia who developed herpes zoster with marked vesiculization, 48 hours later a general vesicular rash broke out on his face, abdomen, legs, and arms The vesicles were not umbilicated He had variola vaccination over 10 years ago On his own initiative, he took a sulfonamide and about 200,000 units of penicillin His blood sulfonamide level, however, was zero Vesicles then appeared in his mouth and about his anus He has been taking 100 mg of corticosteroids daily He now has severe nausea, with vomiting of bloody fluid and distention of his abdomen There is no intestinal obstruction Nikolsky's sign is absent, and there is no eosinophilia What is the cause of this reaction, and what treatment is indicated?*

M D , Wisconsin

Answer —Herpes zoster is a fairly frequent accompaniment not only of chronic lymphocytic leukemia, but also of any of the so-called lymphoblastomas (malignant lymphomas) Cutaneous herpetic lesions may reveal a specific lymphoblastomatous infiltrate or may simply be those of a non-specific or herpetic nature It is unusual, however, for specific or non-specific changes in the cutaneous lesions of herpes zoster to be as generalized as is described in the case in question I do not think that sulfonamide or penicillin are factors in this case Corticosteroids may be a factor Their administration may have to be continued in the treatment of leukemia Discontinuance of corticosteroid therapy for a week or so, if possible, should be considered Cutaneous biopsy would determine whether there is a specific leukemic infiltrate in the herpetic lesions One would not expect to find eosinophilia in the blood of a patient with lymphocytic leukemia I know of no treatment except hospitalization, with good nursing care and measures to alleviate discomfort from the cutaneous lesions, including use of bland lotions and colloid baths

ESSENTIAL HYPERTENSION

To the Editor —*What is the present status of surgical treatment or correction of acquired aortic insufficiency associated with essential hypertension? Also, what surgical group has had the greatest number of cases and the most striking results in surgery for aortic insufficiency?*

Gerald C Haskell, M D , Springfield, Ohio

Answer —It is assumed from this question that the aortic insufficiency is the direct result of the essential hypertension If this is true, no direct surgical treatment of the aortic insufficiency can be effective without relief of the hypertension In the past 10 years, several groups have attempted to reduce the circumference of the aortic annulus by circumferential sutures, but this has proved more hazardous than profitable The proximal segment of the ascending aorta may be banded with various plastic fabrics in an effort to prevent further dilatation, but this does not correct the insufficiency already present

A more satisfactory approach to the problem would be a thorough investigation of the aorta and its main branches, particularly the renal arteries, for a vascular occlusion which could be corrected surgically to improve the hypertension A translumbar, or retrograde, aortogram would be particularly valuable in establishing this diagnosis It must be remembered also that an aortic insufficiency may produce hypertension which is secondary to itself and not essential hypertension In this case a direct replacement of the damaged aortic valve probably represents the most satisfactory treatment This requires an open-heart technique This is still an experimental procedure, with different groups developing new valves Dr Charles Hufnagel at Georgetown University has worked on this problem for many years and his group probably has had more success than any other

HEMORRHOIDS

To the Editor —*What is the current thinking with respect to the injection treatment of external or internal hemorrhoids in the absence of thrombi in the veins? In view of the minor symptoms and a paucity of findings on visual examination, hemorrhoidectomy seems somewhat radical Yet, if the venous sinuses are not promptly relieved manually of the blood distending the veins, thrombi would quickly form*

E D Hockenberry, M D , Coral Gables, Fla

Answer —The injection treatment of hemorrhoids is considered good therapy, within strict limitations Only internal hemorrhoids may be injected *Never* inject external hemorrhoids The internal hemorrhoids must be mild or moderate in severity, non-protruding, and not complicated by fissures or infection Single or multiple involvement may be treated equally well by this method It is not unusual for external perianal veins to fill up during defecation if the patient has had to strain This engorgement usually subsides spontaneously within a short time and should be of no concern Hemorrhoidectomy for small internal hemorrhoids is not indicated and may lead to anal contracture If the external perianal veins, as described by the inquirer in this instance, are troublesome and tend to thrombose repeatedly, careful dissection under local anesthesia would seem to be indicated Further additional details on the technique of hemorrhoidal sclerotherapy may be obtained in any good recent book on proctology

POSTOPERATIVE PYREXIA

To the Editor —*In the last several months, the McKellar General Hospital has had 11 cases of severe immediately postoperative reactions of pyrexia (temperatures of 105 0 to 107 0 F (40 6 to 41 7 C), transient granulocytopenia (leukocyte counts of less than 1,000 per millimeter within a few hours of the reaction, later rising to about 30,000, with 98% polymorphonuclear cells), severe shock requiring intravenous administration of vasopressor drugs in large doses (up to 28 cc of levarterenol per liter for two to five days), mental confusion and agitation of a varying degree, and a marked eruption of herpes simplex in the mouth and circumoral and malar areas after two or three days One patient died Only one patient received a blood transfusion Reactions which may have had a similar cause have been reported after cardiac catheterization A septic abortion, accompanied by vascular collapse, has also been reported Since no positive cause was established in our patients, what other possibilities should be considered?*

G H Morrison, M D , Fort William, Ontario

Answer —Your 11 cases of severe postoperative reactions of pyrexia is certainly unusual and fortunately rare As mentioned, there are many causes for this, and to pinpoint the exact cause is often difficult It would seem that one would have to check the intravenously given fluids for pyrogens and the method of sterilizing the intravenous tubing, in fact, everything which has to do with parenteral medication would have to be checked for a possible pyrogen Unfortunately, as in your patients, the causes are difficult to establish

ULNAR NERVE INJURY

To the Editor —*An elderly woman fell and sustained a subcoracoid dislocation of her right shoulder, this was reduced by traction and mild manipulation Two days later she was unable to extend her right little and ring fingers Where is the possible lesion located? What is the management? When should abduction above the shoulder level be attempted?*

Irving I Crouse, M D , Buffalo, N Y

Answer —Assuming that the hand was normal until the time of the dislocation of the shoulder, the inability to extend the little and ring fingers probably represents involvement of the ulnar nerve originating from injury to the brachial plexus at the time of the dislocation Care also should be taken to ascertain that this is not a more peripherally located lesion, at or near the elbow, arising as a result of pressure from a sling or some other condition at the elbow itself There is also a possibility that inability to extend the little and ring fingers is referable to an acute reflex sympathetic dystrophy, but in such a case the entire hand would be swollen, the palmar fascia would be tender, and there would be color changes

The best initial treatment for dislocation of the shoulder is immobilization for about three weeks with the use of a sling and a swathe Abduction can be allowed as soon as the patient feels able to attempt it, after this time Careful neurological evaluation will decide whether the injury actually involves the brachial plexus, if so, the passage of time and the administration of physical therapy to the involved muscles constitute the usual procedure The possibility of redislocation must always be kept in mind, and if there is any question of this mishap, re-examination by roentgenography is indicated

POST-HERPETIC PAIN

To the Editor —*Please outline the recent advances in treatment of post-herpetic pain in a 70-year-old patient who has had severe herpes zoster*

M D , Michigan

Answer —Post-herpetic neuralgia is still an extremely difficult problem and often remains refractory to treatment From the nature of the query, the location of the pain is uncertain, and this may be important in any attempt to outline a therapeutic regimen Numerous medicaments and therapies have been advocated Aspirin, autohemotherapy, and roentgenotherapy have been most widely used In many instances cobra venom, posterior pituitary extract, Protamide—a colloidal solution of denatured enzyme, and vitamins B_1 and B_{12} are used with mixed results

The use of large doses of the newer psychosedatives has been useful in some cases, but the patient must be carefully observed to guard against complications Immune globulin, too, has been reported to be effective in some instances In many patients, however, despite conservative treatment, the pain persists and surgical intervention may be considered Avulsion of the nerve has been of no value Local infiltrations of procaine and alcohol in the affected areas have not been effective Rhizotomy and cordotomy have been used in some patients with benefit In many instances the pain is severe and persistent enough to warrant psychosurgery

INHALATION OF NOXIOUS FUMES

To the Editor —*Are there any reports of deaths occurring in welders from inhalation of noxious fumes? A patient died of lobar pneumonia within 48 hours of welding a manganese alloy Could the death have been due to welding?*

Philip H Hostetter, M D , Manhattan, Kan

Answer —It is true that welding fumes may contain small amounts of the oxides of nitrogen gas, but Drinker showed that this was present only in trace concentrations which were harmless The early literature reveals only a few poorly authenticated cases of chemical pneumonitis from exposure to extremely concentrated welding fumes The Navy and Maritime Commission shipyards had none during World War II, even while their exhaust ventilation of inner and double bottoms still was not entirely adequate In your patient, the manganese in the alloy being welded could not have been a factor, because manganese is not a bronchial irritant, however, if cadmium plating was involved, this could have caused sufficient bronchial and bronchiolar irritation to have resulted in the lobar pneumonia

CATARACT

To the Editor—*A 52-year-old woman has been taking 2 or 3 capsules daily of A-M Plus, which contains 5,000 units of vitamin A and 5 mg of dextro amphetamine sulfate, for slightly over three years for weight control and a gain in energy In the past six months a cataract has developed in the left eye Is there any connection between this condition and the medication?*

William Thomas Hall, M D, Wilmington, Del

Answer—There is no apparent connection between the development of a cataract and prolonged or excessive use of vitamin A or dextro amphetamine

SUPERVOLTAGE RADIATION

To the Editor—*Our local hospital is equipped with a 200,000-kv deep x-ray therapy apparatus, and our radiologist is competent Recently a wave of interest in radioactive cobalt therapy has swept over our community Patients with cancer have gone elsewhere to receive cobalt therapy Is cobalt therapy superior to deep x-ray therapy, when both are administered by a competent therapist? When a patient asks, "Will cobalt treatments help me more than x-ray treatments?," will I be justified in saying that treatments taken locally will give end-results comparable to cobalt therapy?*

R E Speirs, M D, Dodge City, Kan

Answer—This is a frequently asked question and one which involves several considerations First and foremost, treatment should be given by an experienced and capable radiation therapist While the radiation equipment is of some importance, a capable therapist can do a creditable job with standard orthovoltage equipment Furthermore, he will know when the patient can be better treated by use of supervoltage equipment Cobalt-^{60} teletherapy equipment is only one of the types of supervoltage apparatus The radiation beam should be well collimated, and the treatment distance should be at least 50 cm, preferably more There is a wide variance in the quality of the available types of such equipment Most patients can be satisfactorily treated with orthovoltage equipment If the tumor is deep, if much bone must be traversed by the rays, or if it is advantageous to use a single field only, supervoltage might be preferable

SURGICAL PRIVILEGES

To the Editor—*In order to set up a definite policy with regard to requests for surgical privileges by members of our general practice section, we would greatly appreciate your clarification of any ruling on the following points 1 How do you define major and minor surgical privileges? 2 Should there be an opportunity for advancement with regard to surgical privileges without further or specialized training? 3 Should board eligibility or certification be required for major surgical privileges with regard to new members on the staff and staff members of long standing? 4 Should general practitioners without specialized training be allowed to administer anesthetics?*

Matthew P Lawler, M D, Des Moines, Iowa

Answer—1 In many hospitals the distinction between major and minor surgical privileges is not made Anyone who is privileged to admit private patients may do anything he thinks he is capable of doing 2 When a man is taken on the staff, he has had a full residency in surgery and is eligible for examination by the American Board of Surgery He may therefore perform any operation he feels capable of There is no reason for advancement with regard to surgical privileges 3 Many hospitals do not request board eligibility or certification for major surgical privileges, but it would be a rare exception for a man to have the required training and not expect to proceed to certification Men who have been on the staff for a long time and are not certified by a board are not required nor expected to begin training for certification 4 Many hospitals have a department of anesthesiology, and all anesthesia is given by an anesthesiologist (M D) or an anesthetist In a hospital where such personnel are not available, a general practitioner should be allowed to administer anesthesia

ENTROPION

To the Editor—*Is there some non-surgical solution for the problem of non-cicatricial entropion?*

G Soares Brandão, M D, Monte Real, Portugal

Answer—The expression "non-surgical" presumably rules out the use of instruments, and the term "solution" apparently implies a cure Accepting these premises, it may be stated that there is no non-surgical solution for the problem of spastic entropion

MASSIVE HEMORRHAGE FROM DUODENAL ULCER

To the Editor —*What is the rationale, during performance of an emergency subtotal gastrectomy not touching the duodenum, for a massive hemorrhage from a duodenal ulcer in a man aged 75 years? While the patient was still bleeding, what less formidable procedure might have been performed?*

William S Levy, M D, Woonsocket, R I

Answer —Acute pancreatitis is an occasional complication of subtotal gastric resection For this reason, the duodenum should be handled as gently as possible and special care should be taken to avoid division or ligature of the pancreatic ducts Massive hemorrhage from a duodenal ulcer in a man 75 years of age can be treated by gastric vagotomy combined with pyloroplasty and ligature of the bleeding point Joseph Weinberg and Jack Ferris in Los Angeles have each reported series of patients treated by this more conservative procedure and with an operative mortality much less than that usually associated with subtotal gastric resection The pyloroplasty is performed first, then the ulcer is exposed and ligated with a silk or linen ligature passed through the bed of the ulcer, with use of a figure-of-eight or a mattress type of suture When bleeding has been controlled, blood clots are evacuated from the stomach and the pyloroplasty is completed with a single layer of interrupted silk sutures Vagotomy is then performed in the usual manner and the stomach decompressed by means of a Foley bag gastrostomy Decompression should be maintained for at least five days after the operation

FRACTURE OF FEMUR

To the Editor —*What hazards are associated with use of the Hagie pin in the treatment of femoral neck fractures?*

S C McCrae, M D, Salina, Kan

Answer —Hagie pins are used to immobilize fractures of the femoral neck in the same manner that other types of pins are used The Hagie pins are 6 in long and have coarse threads on the drill point for 1 5 in There are threads on the opposite end to take a hexagonal nut, which is used to tighten it against the lateral femoral cortex They are also valuable in fixing undisplaced fractures or fractures which are to be internally fixed without manipulation when it is undesirable to drive a large nail across the fracture site for fear of displacing the fracture They may also be used to fix a minimal slip of the capital femoral epiphysis They come in two diameters, 1/8 and 5/32 in respectively

They can be drilled into the femoral neck and head without making a preliminary opening in the lateral femoral cortex Although it is usually preferable to have at least three pins across the fracture site, the usual procedure is to place two above and two below the femoral neck, parallel to each other This consultant knowns of no difficulty with migration of the Hagie pins, but there have been some breaks when they are withdrawn by means of a drill, which is reversed in removing the pins Since guide wires are not required, the pins themselves may be used as guide wires and are easily reinserted to attain proper placement and fixation

CONTACT LENSES

To the Editor —*Will the use of contact lenses decrease or stop the progress of myopia or keratoconus?*

M D, Mexico

Answer —There is no scientific evidence that the use of contact lenses will decrease or stop the progress of myopia, nor has it been proved that contact lenses arrest the disease process in keratoconus, but a certain flattening of the tip of the cone during the process of adaptation to the contact lens has been noted It is not known how permanent this flattening is Occasionally, a contact lens may cause the formation of an ulcer on the tip of the keratoconus, resulting in scar formation and flattening of the cornea This may beneficially affect the progress of the keratoconus by strengthening the thinnest area of the cornea

ELECTRONIC FILTERS

To the Editor —*Are electronic filter devices of any value in the removal of allergens from indoor air for patients suffering from mold and pollen allergies?*

Phillip H Starr, M D, Omaha, Neb

Answer —Currently available electrostatic filtering devices effectively remove pollens, fungous spores, and dust particles from indoor air These are available as window units, in cabinet form, or may be installed in the duct systems of air conditioning equipment Since the season of greatest incidence of pollens and spores is the summer, and since the effectiveness of these systems depends on having all the air in a given room pass through this type of system, the combination of electrostatic filtration and air conditioning is much more comfortable than filtration alone None of these devices remove odors and fumes which, in some instances, are also major causes of respiratory symptoms This problem may even be increased by the evaporation of oil-impregnated mechanical filters commonly used in air-conditioning equipment Although such odors may be removed by incorporating activated carbon filters, commercial equipment containing sufficient activated carbon for this purpose is not generally available

ABSTRACTS FROM THE LITERATURE

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Nodular Dermal Allergid—Inflammation of the arteries in various organs leading to hemorrhage followed by necrosis (allergic vasculitis) gives rise to several diseases which vary greatly as far as their clinical features are concerned If the cutaneous arterioles and capillaries are affected, there may be polymorphous cutaneous eruptions without interference with the general health This includes certain cases of purpura, the nodular dermal allergid (Gougerot), and allergic arteriolitis (Ruiter) In the advent that the medium-sized arteries of the skin are involved, the term cutaneous periarteritis nodosa has been applied Where the arteries in organs other than the skin are affected, various syndromes have been described These include periarteritis nodosa, allergic granulomatosis, Wegener's granulomatosis (pathergic granulomatosis), and temporal arteritis, most of which have a serious prognosis and eventuate in death The cause of this allergic vasculitis is unknown There is no satisfactory treatment

Treatment of Vascular Component of Psoriatic Lesion—This study was undertaken to determine the effect of therapy on the capillary abnormality which has been well-documented as being an important component of the changes characteristic of psoriasis Psoriatic lesions were observed to completely involute after the use of 4 different therapeutic regimes (1) crude coal tar and ultraviolet light daily, (2) amethopterin, 2 5 mg daily for 1 week, alternating with 1 week of no treatment, (3) x-ray therapy to localized lesions, and (4) triamcinalone in various dosages Despite clinical inability to make a diagnosis of psoriasis after therapy, all patients still demonstrated the highly characteristic elongated and tortuous capillaries in areas where psoriatic lesions were known to have existed

Pityriasis Alba—In a study of 67 patients with pityriasis alba the sexes were involved almost equally, and the lesions usually involved the face alone or the face, neck, arms, and shoulders Eight patients had generalized lesions Pityriasis alba is considered to originate as a non-specific erythema of unknown cause but with some relationship to asteatosis No evidence was found to support the role of fungi or bacteria as etiological factors The influence of seasons and climate were uncertain Follow-up data, available in 32 patients, showed that clearing or improvement was independent of the type of medication used Dryness of the skin was the only consistently aggravating factor

Efficacy of Some Ambulatory Dermatological Therapies—The efficacy of ambulatory (office) management of 10 common dermatoses in 1947-48 and in 1957-58 was compared The criteria of efficacy were the number of office visits and the total time needed for cure or control of the dermatoses Twenty to 25 relatively comparable patients out of 251 patients in each diagnostic category in 1947-48 and out of 260 patients in 1957-58 were considered For the entire group of patients 1 5 fewer office visits and 11 5 days less of total treatment time were required for cure or control of the 1957-58 group in comparison with the 1947-48 group In those dermatoses known or thought to be hypersensitivity reactions, the differences in necessary treatment times and office observations were considerably greater (2 2 fewer observations needed and 19 days less of total treatment times) The differences were found to be statistically significant It is suggested that, in large measure, the increased efficacy of 1957-58 dermatological treatment has resulted from the advent of steroid medications

Curettage and Electrodesiccation in Skin Cancer—Curettage and electrodesiccation were employed as the method of treatment for 765 epitheliomas of the basal and squamous cell types For all 765 lesions the cure rate was 98 3%, with the maximum follow-up being 19 years and the minimum being 6 months In the group followed for 5 years or longer, the cure rate was 96 67% Results with squamous cell carcinomas were equal to those obtained with basal cell epitheliomas Recurrences presented no problem in retreatment and there were no metastases nor deaths This method of treatment has not received proper emphasis in medical literature and has been unjustly criticized by some physicians Our results with curettage and electrodesiccation compare favorably with those obtained by other methods used to treat skin cancer

Staphylococcal Infections—In a 9-month clinico-bacteriologic study of 306 unselected, successively hospitalized patients with cutaneous diseases, an incidence of 8 8% (27 of 306) of complicating staphylococcal infections was found Analysis of relevant and interpretable data suggested that the following factors were promotional (1) prophylactic administration of antibiotics, (2) administration of adrenocorticosteroids in any amount, particularly in high doses and long maintenance, (3) the character of the dermatosis in terms of prognostic seriousness and debilitating effect on the system as a whole, and (4) hospitalization of 2 weeks or more Of the 27 cases of staphylococcal infections 20 were furuncular 6 were septicemias (4 fatal), and 1 was bronchopneumonia (fatal) In the fatal cases the microorganisms were phage type 80/81 in 4 and 53, VA 4 in 1 The other significant finding was that banal cutaneous diseases, in themselves, were not particularly infectable

Fox Fordyce Disease in Male Identical Twins —The purpose of this report is to document the unusual occurrence of Fox Fordyce disease in young male identical twins Important histopathological and histochemical findings were the presence of giant cells, some of the Langhans type located in periductal sweat retention vesicles In the papillary dermis there was a mucinous material identified as predominantly hyaluronic acid or chondroitin sulfate or both Another material was present, both free and within histiocytic foam cells, associated with granulomatous foci at sites of apparent rupture of the apocrine glands and ducts This material, most likely a saturated bound lipoprotein, has been demonstrated to be a constituent of normal apocrine glands The occurrence of the disease in identical twins supports the concept of nevoid origin or predisposition to development of the disease The histochemical findings suggest an endocrinologic or metabolic disorder

Ars Longa, Vita Brevis —When Hippocrates enunciated his 1st aphorism The art is long, life short medicine had little more than the art to offer We now have art and science, but our training as physicians is concerned almost entirely with the latter Our patients, however, expect from us more than scientific knowledge skill, and clinical judgment in the much discussed physician-patient relationship, they take all that for granted when they choose a physician Our patients need and expect sympathy understanding and intellectual honesty in the physician of their choice It is suggested that a thorough grounding in the humanities during premedical education and continuous follow-up in these areas of thought and knowledge throughout our medical training would better prepare us and future physicians to render the type of medical attention that our patients need for complete satisfaction

Amyloidosis A New Clinical Type —This report dealt with a single case of a 12-year old male with yellowish nodular skin lesions about the face and neck These appeared after excessive sunlight exposure The gross appearance of these lesions was compatible with the condition known as colloid milium Histological examination, however revealed the subepidermal deposits to be amyloid Further examination revealed no evidence of other disease or of any additional amyloidosis The chemical similarity of colloid and amyloid was noted as well as the fact that both materials appeared in the skin under conditions associated with tissue degeneration From this remarkable and extensively studied case it is concluded that amyloidosis and colloid milium may be closely related conditions

Divided Nevus —A case is presented of a divided nevus a rare morphologic variant of nevus pigmentosus The term divided nevus has been used by ophthalmologists to describe pigmented nevi which straddle the upper and lower lids and form a continuum when the lids are closed Assuming that this dual lesion originally arose from a single focus (an assumption made almost certain from the configuration of the lesion with the lids in apposition), it is shown that its time of origin must have been during the period of lid fusion in fetal development, corresponding approximately to the 2nd trimester of gestation Studies showing the 1st appearance of melanocytes during the period of lid fusion are cited to give further support to this thesis Using the divided nevus as a case example, the authors conclude that pigmented nevi may arise as early as the 2nd trimester of gestation

Reactions in Green Tattoos —Reaction in a green tattoo occurred after acquiring eczematous dermatitis on contact with cement As in 5 of the 7 previously reported cases, patch tests to bichromates were positive The affected green portions of the tattoo were excised and the chronic eczematous areas on other parts recovered promptly Histologically the green tattooed areas showed adjacent sarcoid and nonsarcoid types of foreign-body granulomas Simultaneous sensitivity to bichromates and to the chrome green used in tattooing is not an adequate explanation for reactions in green tattoos as the former are sexivalent and the latter trivalent chrome compounds, patch and prick tests with trivalent chrome were consistently negative, and the possibility of cross sensitization is rejected Oxidation in situ of trivalent to sexivalent chrome is thought to be unlikely, and it is thought that the presence of a trace of sexivalent chrome as an impurity in the tattoo pigment provides the most likely explanation

Demethylchlortetracycline —In our study of 70 patients treated with demethylchlortetracycline who had pustular dermatoses, ranging from acne rosacae to impetigo, it was found that the over-all results were good to excellent In acne vulgaris demethylchlortetracycline results compare favorably with those of oxytetracycline and tetracycline In our opinion the former drug is superior, it most surely is if analyzed milligram for milligram with the 2 latter drugs An unexpected and unique side effect not previously reported was observed in 7 of our patients The reaction is a contact eczematous type manifested by brilliant erythema with edema on exposed areas We feel these reactions are photodynamic dermatoses, energized by blue light or by a wave length of light longer than 3900 A up to visible light

Herpes Zoster Trigeminal Neuralgia —Six cases of acute herpes zoster trigeminal neuralgia, involving 1 or all 3 branches of the trigeminal nerve, seen in our office within the past 3 years have obtained relief from pain by alcohol block of the great occipital nerve in the ipsolateral side No recurrence of neuralgia was experienced in any of these cases It was our impression that these zoster lesions subsided more rapidly than those treated by other methods This simple technique, which is described in detail, can be performed in the office The authors used from 3 to 5 ml of 95% ethyl alcohol for injection purposes without any local tissue effect noted We feel that this procedure may be worthy of trial in cases of herpes zoster with trigeminal neuralgia and in those cases of tic douloureux when surgery is not indicated

Oxytalan Fibers of Dermal-Epidermal Junction —In a study of 100 cutaneous biopsy specimens from 70 patients with various dermatological diseases it was found that fine fibrils which stained with peracetic acid-aldehyde fuchsin could be found consistently at the dermal-epidermal junction These fibrils were present at the dermal-epidermal junction even in conditions showing some destruction of the elastic fibers postplaned skin of the face, keloid, postradiation scar, discoid lupus erythematous scar, and late scleroderma

Basal Cell Epithelioma of Palm—This is a report of a basal cell carcinoma in an unusual site, the thenar eminence of the palm of a white man 70 years of age, illustrated with a clinical photograph of the tumor and representative microphotographs of its histopathology A review of the literature revealed that approximately 96% of all basal cell carcinomas occur above the level of the clavicles on the face or neck A few basal cell epitheliomas of the sole had been reported previously No other case of basal cell epithelioma of the palm was found in the literature

Disseminated Vaccinia in Pregnancy—A 23-year-old pregnant negro female with atopic dermatitis who had been exposed to the vaccination lesions of her children developed an acute vesiculopustular eruption of face and neck with fever, headache, and general malaise The combination of her skin affection plus the pregnancy at term added up to a serious situation with an almost fatal outcome At the height of her disease she gave birth to a healthy male infant who showed no signs of the disease and whose skin remained clear The patient's skin lesions healed with complete depigmentation which was followed by full repigmentation within 1 month

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Skin Soiled by Radioactive Materials—The removal of radiophosphorus and radioiodine from human skin by use of granulated and waterless skin cleansers was studied A protective lotion lanolin or silicone, was used on some test areas to determine if it facilitated decontamination With a group of experimental subjects comprised of 92 men and 63 women, removal efficiencies of 99.6% for the P_{32} and 99.0% for the I_{131} were demonstrated This high degree of removal was effected with the granulated skin cleansers, the waterless types being less efficient in their action The protective property of the silicone and lanolin lotions was not demonstrated in this experiment

Study of Carbon Tetrachloride—The present report is a study of the relationship of serum and liver glutamic-oxaloacetic transaminase (GOT) esterase and xanthine oxidase activity following a high level of exposure to carbon tetrachloride vapor Twenty-four hours after exposure, serum esterase was 160% of control levels (100%), while liver esterase was only 20% of its original value Xanthine oxidase activity in serum increased to 1100% and liver xanthine oxidase decreased to 40% of control levels Twenty four hours after exposure, serum GOT had increased to 55 times its control levels and liver GOT to 180% of normal values The elevated serum enzyme levels returned rapidly to normal, indicating a prompt inactivation or removal of these enzymes from the blood stream The liver enzyme activities returned to normal at a somewhat slower rate (3 to 5 days)

The Metabolism of 1,1,1-Trichloroethane in the Rat—The purpose of this study was to determine the metabolism of 1,1,1-trichloroethane, industrial solvent and anesthetic, by the intraperitoneal injection of 1,1,1-trichloroethane-1 C^{14} into the rat Three adult albino rats were studied After injection the animal was placed in an all-glass metabolism chamber for 25 hours Analyses of the expired air for $C^{14}O_2$ and unchanged 1,1,1-trichloroethane-1-C^{14}, and radioactivity analyses of urine, feces, and various tissues were performed It was found that 98.7% of the radioactivity in the dose appeared as unchanged 1,1,1-trichloroethane-1-C^{14} in the expired air 0.5% was converted to $C^{14}O_2$ and 0.5% was identified in the urine as the glucuronide of 2,2,2 trichloroethanol-2-C^{14} It was concluded that the rat almost totally excretes 1,1,1-trichloroethane via the lungs as the unchanged material, while a trace is metabolized to 2,2,2-trichloroethanol and CO

Trichloroethylene Effects on Animal Behavior—We have studied the effects of exposure to trichloroethylene vapor on rats conditioned to climb up a rope in order to reach a feeding trough where they found a reward, a sugar pellet Previous exposure to 200 and 800 ppm of solvent did not modify either the conditioned responses or the response time of the animals On the other hand, the spontaneous climbs, without previous signals, were significantly more frequent in the exposed rats than in the control rats This observation permits the conclusion that trichloroethylene in the doses studied modifies the psychological equilibrium of rats in the sense of a disinhibition or of an increased excitability

Massive Pneumoconiosis from Rock Dust—Nearly all of the inorganic dusts which have been reported as causing pulmonary fibrosis contain some free silica This report concerns a man who, over a period of 4 years, had inhaled much dust from nepheline rock which contains no free silica He died of respiratory insufficiency, following an operation from another complaint, and at necropsy his lungs were firm and white from deposits of nepheline dust in histiocytes in the lymphatic pathways Assay of the lungs showed silicate to be 54.7% of the ash Free silica was absent In some areas there was consolidation caused by organized and organizing intra-alveolar exudate with foci of frank necrosis and much obliterating hyperplasia of the pulmonary arteries This change corresponded with the massive pneumoconiosis found with other dusts and proved that free silica is not necessary for the development of this lesion The authors attributed the massive lesions to recurrent attacks of broncho-pneumonia which had failed to resolve because of the lymphatic block No evidence of tuberculosis was discovered

Occupational Disease, Pesticides and Chemicals—This analysis of reported occupational disease attributed to pesticides and agricultural chemicals showed that these chemicals are creating an increasingly important public health problem California law requires physicians to report to the Department of Industrial Relations all occupational injuries, including disease The State Department of Public Health receives those reports dealing with disease and analyzes them for public health implications In 1957 the Department analyzed 19,000 such reports, of which 749 were attributed to pesticides and agricultural chemicals The disproportionate effect of the organic phosphate pesticides was brought out in that over 30% of the 749 reports and 75% of the 252 reports of systemic poisoning were attributed to them The analysis was done by geographic area, industry, occupation time lost from work, age, and fatalities

Health of Workers Making Highly Dispersed Silica —A 12 year old plant makes colloidal SiO_2 of 99 8% purity Particle size ranges from 5 to 40 mμ and shows normal specific surface area of 100 to 450 sq m per gram A total of 215 workers have been examined with 720 chest x-rays Although dust concentrations where most men are exposed are in the 2 to 7 mg per cu m range, careful examinations indicate no ill effects of any kind, no respiratory embarrassment and no lung changes

Epidemiologic Methods in the Study of Silicosis —Although silicosis continues to be a major occupational hazard in the United States, present control of this disease is based on epidemiologic studies which may be misleading The authors used a research project in the Vermont Granite Industry to illustrate techniques of modern, chronic disease epidemiology in studying silicosis Period prevalence studies, covering 20 to 40 years were recommended rather than point prevalence studies, covering 1 to 2 years, to elicit basic information about the incidence, prevalence, and incubation period of silicosis Periodic radiographs of all granite workers were recommended Each film would then be read by at least 3 observers independently on two different occasions, using standard films for comparative purposes Newer statistical techniques for correlating dust exposure with the severity of silicosis were discussed

Table of Threshold Limit Values for 1960 —A table of threshold limit values, to be used as guides in the control of health hazards in industry, is prepared for publication each year by the Committee on Threshold Limits of the American Conference of Governmental Industrial Hygienists Fourteen substances have been included in the 1960 table which did not appear on the 1959 list of values

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Visual Denotation of Human Sounds —A method for displaying loudness pitch and quality of the human voice has been developed, using the H H Scott sound analyzer The author analyzed the sounds of 23 persons and isolated 4 distinct acoustic patterns (1) Sharp voices of children, hysteriacs, and other immature persons showed concentration of sound energy into 2 adjacent octave bands around 360 cycles per second (2) Hollow voices of aphasics, seniles, and other organically impaired patients had energy concentrated at only 1 point in the frequency spectrum (3) Flat voices of depressed and obsessional patients had acoustic energy spread out indiscriminately over the middle frequency range (4) Robust voices of aggressive and outgoing people showed a symmetrical distribution of acoustic energy These patterns are plotted on prepared graph paper and can be kept in the patient s chart for objective study Sounds made by patients often provide valuable diagnostic clues With this method of visual denotation the physician can define the voices of his patients without having to use word descriptions or listen to tape-recordings

Husbands and Treatment of Schizophrenic Women —In studying the reactions of 43 husbands of women who were hospitalized for schizophrenic illnesses, the authors became increasingly aware of the need to determine means of effectively integrating the husband into his wife s treatment program We aimed at helping the husband to feel that his interest and cooperation were a vital part of the therapeutic program and at understanding the difficulties that confronted him in his interactions with his wife Characteristically different problems arose in different phases of the wife s course in the hospital admission phase, the phase of acclimation and reintegration, the phase of integrated communication in therapy, and the pre-discharge phase With no impairment of doctor-patient relationship we developed a good rapport with the husband which broadened and enriched our understanding of the total picture

Semantics and Context of Schizophrenic s Language —The schizophrenic s language is discussed in terms of its semantics and of its context, i e , the human relationship in which the language was used The schizophrenic has categorized and symbolized his early experiences differently from the prevalent culture or has altered the normal symbol-referent conjunction by attaching the symbol (word) to a different referent or by denoting anew (neologisms, foreign words, numbers, etc) the old referent A pathologically asymmetrical relationship with the mother-figure is the context within which and about which the schizophrenic speaks though in fear of being understood Backed by illustrative clinical material, the author hypothesizes that in the safety of a highly personalized code the schizophrenic finds not only a way to vent forbidden feelings but also finds the satisfactions of independence and self-assertion otherwise denied to him

Hydroxyzine Hydrochloride and Performance of Schizophrenic Children —Fourteen schizophrenic and 24 normal children were studied to examine their responses to sound and light in terms of reaction time, modality shifting and set formation The schizophrenic children were examined before and during the administration of 60 mg of hydroxyzine hydrochloride daily and compared to the normal children who received no drug Schizophrenic children have significantly longer reaction times than normal children to both sound and light Under the influence of the drug the reaction time of schizophrenic children approached that of the normal children While normal children established sets to both light and sound the only set established by schizophrenics was during their response to a light stimulus in the predrug condition. Reduction in fear and behavioral disturbance in the testing situation emerged in the postdrug condition. These findings are providing hypotheses for further studies.

Interaction Chronograph Method.—We have adapted an objective method, the interaction interview, for the quantitative analysis of schizophrenic behaviour. The function of this interview was to obtain measurements of interpersonal relationships in units of time. This measurement of time had 3 relevant aspects: the actions, silences, and maladjustments of the subject. These aspects were brought out by the juxtaposition of stress and stress-free periods within the interview. Analysis of the data showed that schizophrenic and *normal* subjects were differentiated in terms of interaction variables expressed in units of time. The data may be used to characterize behaviour without recourse to the currently popular psychodynamic formulations, thus introducing an instrument for the objective evaluation of psychopharmacological therapy in man.

Character Defense Preference and Group Therapy.—Six nursing students who constituted a psychotherapy group were *intensively evaluated through psychological tests* and interviews and classified according to their primary defense mechanism. There were 3 deniers, 1 repressor, 1 obsessive-compulsive, and 1 projector. All verbalizations during 18 hours of meetings were rated as positive, negative, or neutral. The 3 deniers participated in a more positive than negative fashion, missed the least number of sessions, and had the 3 highest percentages of non-hostile comments. The repressor made more use of extreme positive and negative categories and showed the greatest range of negative verbalizations session to session. No significant difference occurred between the number of positive and negative statements for the repressor and projector. The obsessive-compulsive expressed more negative than positive statements.

LSD and JB 318: 2 Hallucinogens.—In a counterbalanced design 4 psychological tests were administered to 10 medical students before and after 100 mcg of lysergide (lysergic acid diethylamide, or LSD) and 15 mg of N-ethyl-3-piperidylbenzilate hydrochloride (JB 318). Findings on the Minnesota Multiphasic Personality Inventory (MMPI), tape-recorded pre- and postdrug interviews, and the Jarvik Questionnaire were described in Part I of this series. This paper deals with Rorschach and Clyde Mood Scale data. Neither drug induced major quantitative changes in the classical or DeVos-Rorschach variables. DeVos anxiety and body-preoccupation responses were significantly correlated with behavioral effects of JB 318, hostile and neutral responses with lysergide effects. JB 318 induced profound changes in 6 of 7 Clyde Mood Scales and lysergide in 2.

Psychodynamics of Consummated Maternal Incest.—Two cases of consummated maternal incest are reported, 1 in which *the son* was actively seduced by the mother, the 2nd in which the converse occurred. Both patients became actively schizophrenic. The following factors appear to be associated with the failure of the incest taboo to prevent actual consummation: (1) lessened propinquity due to an intensely rejecting mother, (2) absence of the same-sexed parent in the home, (3) overt maternal seduction, (4) loss of maternal control, (5) slight age discrepancy between mother and son, (6) witnessing the primal scenes, (7) other incestuous experiences with members of the family, (8) intensified sexual frustration, (9) low intelligence, (10) undue physical contact by the mother, and (11) less incest taboo in non-consanguineously related parents. There is a considerable body of clinical evidence to show that repressed incest conflict plays a large and generally neglected role in the genesis of severe personality conflicts, particularly those productive of schizophrenia.

Adolescent and Young Adult Self-Mutilation Incidents.—This study analyzed 90 self-mutilation incidents in 12 patients (ages 14-22). The patients constituted 3 diagnostic categories: 5 severe character disorders, 4 schizophrenics, and 3 borderline states. Three *foci were examined*: (1) the individual patient, (2) both formal and informal group formations, and (3) attitude of personnel (therapists and *nurses*). *We found that the* self-mutilation incidents were suicidal gestures rather than suicidal attempts, with 1 exception. *They* were *related to a conscious* wish such as attention-seeking, prestige-gaining, or tension reduction. The major psychodynamic factor was aggression turned against the self. The self-mutilation incidents had hospital-wide repercussions and were imitated by other patients. They were accompanied by considerable disruption of communication channels within the hospital. It is important to note that an endemic situation like self-mutilation, which one finds in every psychiatric hospital, can turn into an epidemic-like situation in the highly organized setting of a general psychiatric hospital.

Psychoses in Systemic Lupus Erythematosus.—Psychoses were found in 26 of a series of 53 patients with systemic lupus erythematosus (SLE). The majority of these patients had an organic brain syndrome secondary to the disease itself. Steroids were implicated in producing a psychotic reaction in only a small minority of the cases. Other psychotic categories were schizophrenia and psychotic depression. Depressive reactions were a common nonpsychotic finding. The organic mental syndrome occurred relatively early in the course of the disease, most often during or immediately after an acute exacerbation; this should not be considered a terminal manifestation, though it is associated with a poorer prognosis. Treatment with steroids may be essential in alleviating both medical and psychiatric symptoms in the majority of patients. In the presence of lupus activity, mental disturbance is not a contraindication to steroid therapy. Tranquilizers and electroshock were found to be useful therapeutic adjuncts.

American Journal of Medicine, New York

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The Virus Theory of Leukemia p. 683
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The Anemia of Leukemia.—The authors discuss the pathogenetic mechanisms, clinical manifestations, and treatment of anemia in the various forms of leukemia in which anemia is a common complication. Cases are cited to illustrate the abnormalities of the red cells produced in hypoplasia of the bone marrow which is now recognized as a preleukemic state in patients who develop leukemia and myeloid metaplasia Particular reference is made to the role of hemolytic mechanisms In some patients, notably in those with acute leukemia and myeloid metaplasia, abnormalities in the shape of the red cells, i e , poikilocytosis, spherocytosis, and leptocytosis, with corresponding abnormalities in osmotic fragility, may be striking In other patients extracorpuscular factors appear to be largely responsible for hemolysis The most clearly identified examples of such factors are the autoantibodies observed in patients with chronic lymphocytic leukemia Other extracorpuscular hemolytic agents or mechanisms are operative in leukemia but cannot be identified as yet. Inability of the bone marrow to respond to increased demands for erythropoiesis imposed by accelerated destruction of red cells or by blood loss or both, is a general pathogenetic mechanism observed frequently in leukemia of all types The observations cited emphasize the fact that the leukemias are a group of diseases in which the cellular abnormalities are by no means confined to the leukocytes

Clinical Management of Leukemia—Empirical systems of treatment, employing chemical agents and irradiation in a manner specified for each type of leukemia, can relieve symptoms and offer the chance of an extended period of relative well-being to patients with leukemia The use of whole blood transfusions and antibiotics, as the indications arise, is important if the best result is to be achieved Treatment of acute lymphocytic (lymphoblastic) anemia with 3 main classes of agents, namely steroids, the folic acid antagonists, and the purine antagonists, frequently produces full remissions and, compared to untreated patients, at least a twofold increase in the duration of life after the onset of symptoms In contrast, in the treatment of acute granulocytic (myeloblastic) leukemia, neither full remission nor prolongation of life occurs frequently, although some benefit is sometimes obtained Therapy of chronic myelocytic leukemia using irradiation and administration of busulfan (Myleran) may produce full remission with great regularity, however, an accompanying prolongation of life has not been reported in most series In chronic lymphocytic leukemia irradiation and chemotherapeutic agents such as chlorambucil, triethylene melamine, nitrogen mustard, and steroids may produce remissions which are often not as complete as in chronic myelocytic leukemia, but symptoms are often less severe, the disease is more indolent, and, in the experience of some workers, longevity is greater

Transplantation of Human Bone Marrow in Leukemia—Twenty-six attempts at transplantation of human bone marrow obtained from ribs resected from patients without a malignant or infectious disorder and from voluntary healthy donors were carried out in 19 patients with acute leukemia and other marrow depletion syndromes with or without preliminary treatment with total body irradiation The bone marrow suspension was slowly injected into the tubing of an intravenous isotonic sodium chloride solution infusion set, previously inserted into an arm vein There was no evidence of a permanent take after any of the attempts, although signs of transient functioning of the bone marrow appeared in 3 patients Four additional patients, 1 with malignant lymphoma, 1 with aplastic anemia, 1 with reticulum cell sarcoma, and 1 with mycosis fungoides received intravenous infusion of bone marrow aspirated from bones of volunteer donors (homologous marrow) or from the patients themselves (autologous marrow) The patient with reticulum cell sarcoma underwent a relatively long remission after receiving 100 mg of nitrogen mustard followed by injection of her own preserved marrow The course of the patients with acute leukemia did not in general seem to be altered significantly by irradiation and injections of bone marrow These methods of processing marrow procured from ribs and vertebral bodies excised from patients, from voluntary healthy donors, and from cadavers of recently deceased persons and of administering the marrow to patients may provide a basis for the utilization of human bone marrow in future attempts to transplant bone marrow

Annals of Surgery, Philadelphia

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Benign Neoplasms of the Gallbladder—The authors discuss observations on 45 patients with benign neoplasms of the gallbladder, which were observed over a period of 15 years at the Ochsner Clinic in New Orleans Cholecystographic discovery of these tumors is becoming more frequent, since modern roentgenographic techniques may disclose them when they are only 2 or 3 mm in diameter The presence of a fixed radiolucent defect in the opacified gallbladder is suggestive, while it may mimic a radiolucent gallstone, the constant position suggests a tumor, because a gallstone usually moves around Benign neoplasms of the gallbladder produce no specific manifestations Gaseous indigestion and upper abdominal pain, the most frequent complaints in the patients reviewed, are so common that they are difficult to evaluate The dilemma facing the patient with a suspected benign tumor of the gallbladder is whether to undergo a cholecystectomy The authors advocate this operation because malignant tumors may arise from benign tumors The gallbladders of all 45 patients were removed, and there were no operative deaths and no significant postoperative morbidity There were 18 patients with adenoma, 15 with papillary adenoma, 9 with adenomyoma, 2 with non-invasive carcinoma, and I with fibroadenoma Fourteen of the patients had multiple lesions, 21 had gallstones, and in 34 the gallbladder showed chronic cholecystitis

Significance of Discharge from the Nipple—A hemorrhagic or serosanguineous discharge from the nipple usually indicates a pathological process involving the breast ducts There are 2 schools of thought in regard to its significance One stresses the frequency with which cancer of the breast may be associated with such a discharge The other school stresses the frequency with which benign conditions, such as intraductal papilloma, produce bleeding The authors review observations on 67 patients with discharge from the nipple, who were found among 810 patients with breast disease followed-up in the Department of Oncology, Georgetown University Hospital Washington, D C, from 1947 to 1959 The nipple discharge was bloody in 27 and serous in 40 of the patients There were 24 women with breast cancer, 1 man with neurogenic sarcoma of the breast, and 42 women with benign breast lesions In the patients between 20 and 49 years of age nipple discharge was associated with benign lesions more than twice as often as with malignant lesions (37 and 15 patients, respectively) Among the patients over 50 years of age discharge from the nipple assumed an increasingly serious significance Cancer was found in 8 of the 11 patients over 50 years of age who had a bloody nipple discharge A breast with nipple discharge but without a palpable mass must be suspected of harboring a cancer or a precancerous lesion (intraductal papilloma, adenosis) until this has been disproved Treatment includes (1) close observation and follow-up, (2) progesterone therapy in selected cases, (3) local excision of lesion or of localized parenchymal source of bleeding, (4) simple mastectomy under certain conditions, (5) radical mastectomy if cancer is found

Arquivos de neuro-psiquiatria, São Paulo

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Cerebral Granuloma from Blastomycosis
O Lemmi and A M Pimenta p 58

Neurologic and Electrolytic Side-Effect of ACTH —A 10-year-old boy was hospitalized with *nephrotic syndrome* and subjected to treatment with ACTH and potassium chloride together with low-sodium diet A total of 825 mg of ACTH was given by intramuscular injections On the 4th day of treatment a diuretic phase started accompanied by diarrhea Extrasystoles were observed on the 8th day, and tonic-clonic convulsions developed on the 10th The administration of ACTH was then discontinued The patient passed into coma, remaining unconscious for 22 days Electrocardiographic changes, hyponatremia, hypokalemia, hypochloremia, and alkalosis developed Treatment consisted of hyperproteinic and hypercaloric diet by gastric intubation, together with compensatory administration of fluids The patient improved gradually and, 3 months later, received prednisone (15 mg daily), chlorothiazide, and potassium chloride (2 Gm daily) When he was discharged, 8 months after admission to hospital, the sequelae of convulsive episodes and right lateral hemianopsia still persisted The need for periodic determination of the electrolyte level during ACTH therapy and for intravenous administration of potassium at the first sign of electrolytic disorder is emphasized

Cerebral Granuloma from Blastomycosis —In addition to the usual complications of South American blastomycosis, a condition which tends to invade the whole system of the patient, several cases of neurologic involvement have been reported A 62-year-old man complained of headache of 2 months' duration, nausea, dizziness, and a spell of total amaurosis He had been treated with sulfonamides for leishmaniasis and blastomycosis during 8 years, but sputum examinations remained positive for Blastomyces brasiliensis As electroencephalographic and cerebrospinal fluid examinations confirmed the presence of cerebral damage, craniotomy was performed, and a hard, dark, irregular mass, deeply located in the frontal lobe, was removed Bacteriological and histological studies established the diagnosis of cerebral blastomycosis The patient died 5 days after the operation, although the immediate postoperative period had been uncomplicated

Journal of Bone and Joint Surgery, London

42B 1-174 (Feb) 1960 Partial Index

Radioactive Isotopes in Fractures of Femur
G P Arden
Arthroplasty of the Knee p 21
L G P Shiers
Hemangiopericytoma Orthopedic Manifestations p 31
J C Kennedy and J H Fisher
p 80

Arthroplasty of the Knee —The author performed 28 operations for arthroplasty of the knee on 17 patients ranging in age from 55 to 75 years Fourteen had osteoarthritis and 3 were suffering from the late effects of rheumatoid arthritis In 8 knees a good result followed the primary hinge operation and remained good up to the time of follow-up (average 46 months) The original prosthesis proved to have a potential weakness at the joints where the intramedullary stems were screwed into the hinge halves Fracture of the prosthesis at 1 of these points occurred in 7 knees after intervals of from 4 to 40 months after operation In 5 of these a good result followed replacement with a new prosthesis and remained good up to the time of follow-up (average 23 months) According to experience the author modified the prosthesis by considerably shortening the stem and by enlarging the diameter of the locking screw It is possible that with the modified prosthesis successful results could be obtained in 3 out of 4 cases The operation may have a place as part of a program of salvage in cases of affection of many joints

Hemangiopericytoma —The author reports 9 patients with hemangiopericytoma, the malignancy of which has been underestimated in the past The appearance of a painless lump, increasing in size on the trunk or extremities, which may feel encapsulated and which is devoid of inflammatory reaction should cause the clinician to consider hemangiopericytoma in the differential diagnosis The course of hemangiopericytoma is unpredictable because it infiltrates locally, has a high incidence of local recurrence and a varying rate of metastasis Wide local and radical excision of the tumor is the treatment of choice, and if there is evidence of recurrence after removal of the tumor from the thigh amputation should be performed The prognosis in regard to malignancy appears to be worse when the tumor is in the lower limb The incidence of hemangiopericytoma is greater in the first half of life Of the 9 patients in this series 6 were under the age of 30 years All the 9 patients were subjected to operation, 6 had a recurrence of the tumor after local excision, 4 developed metastases and died, 2 of these were given cobalt ^{60} beam radiation treatment Five of the patients showed no evidence of recurrence at the time of follow-up (for the period of 1 to 2 years), 2 of these received cobalt ^{60} beam radiation therapy

Journal of Pathology and Bacteriology, Edinburgh

79 221-448 (April) 1960 Partial Index

Properties of Staphylococci Related to Pathogenicity p 237
J Brown
Effects of Diphtheria Toxin on Acetylcholine Synthesis p 315
S C Agarwal

The Great Veins in Venous Hypertension
M Stuart and F R Magarey p 319
Effect of Anesthesia on Renal Ischemia
H L Sheehan and J C Davis p 337
Congenital Cystic Disease of the Lungs
A D Moffat p 361

Properties of Staphylococci Related to Pathogenicity—Pathogenic strains of staphylococci are generally recognized by means of the coagulase test, but many workers have shown that there is a correlation between alpha-hemolysin production and pathogenicity in human strains The author describes studies that were undertaken to ascertain the usefulness of alpha hemolysin production as a criterion of pathogenicity, to examine alpha-hemolysin production quantitatively, and to determine the number of antigen-antibody lines formed and the hemolytic patterns of strains in various staphylococcic lesions from human sources Some of the properties of 400 strains of coagulase-positive staphylococci isolated from human lesions were examined There was a direct relationship between the amount of alpha-hemolysin produced by each strain and both the number of antigen-antibody flocculation lines formed and the complexity of the hemolytic pattern Strains from acute lesions in apparently undamaged skin tended to produce more alpha-hemolysin and more flocculation lines than those from burns and postoperative wounds, and these in turn produced more alpha-hemolysin and more flocculation lines than strains from the urinary tract Though coagulase production may well be necessary for the pathogenicity of a strain, it is suggested that the degree of virulence of a staphylococcic strain can be most conveniently estimated by its alpha-hemolysin production

Journal of Urology, Baltimore

83 511-784 (May) 1960 Partial Index

Renal Bivalving for Differentiaton of Kidney Lesions
T Mason and W B Crenshaw p 539
Concomitant Renal Infarction and Pelvic Papilloma
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J E Dees p 550
Permanent Nephrostomy or Permanent Cutaneous Ureterostomy
M Wosnitzer and J K Lattimer p 553
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C L Prince and P L Scardino p 561
Ureteral Diverticula
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Benign Polyp of Ureter
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Use of Bladder Pedicles as Substitutes for Lower Ureter
J R Dillon Jr p 583
Pheochromocytoma of Urinary Bladder
W W Scott and S L Eversole p 656

Bivalving for Differentiation of Kidney Lesions—The surgeon who contemplates nephrectomy for a suspected tumor may encounter an apparently normal kidney In this dilemma he has several alternatives (1) If palpation fails to reveal any abnormality he may close the wound, but an occult neoplasm may be overlooked (2) He may remove tissue for biopsy, but a positive diagnosis is possible only when neoplastic tissue is found (3) He may remove the kidney, but nephrectomy may needlessly sacrifice a kidney with a benign lesion (4) He may bivalve the kidney through the suspicious area This report emphasizes diagnostic bivalving (nephrotomy) for renal exploration The vascular supply of the kidney makes bivalving feasible There is a line (Broedel s line) in the long axis of the lateral border in which there are no large vessels Section of the kidney through this area is safer than other nephrotomy incisions which transect branches of the larger interlobar or interlobular arteries The authors bivalved 14 kidneys for diagnostic purposes In only 1 of these was tumor found Intrarenal cysts were discovered in 7 patients, and treated by local excision Aberrations of renal architecture were found in 5 cases, and no treatment carried out A renal infarct caused 1 abnormality In all patients except those with the infarct and the tumor, the kidney was salvaged and returned to normal function The patient with renal infarct had secondary nephrectomy, the renal tumor was treated by immediate nephrectomy Disadvantages of bivalving include the possibility of delayed hemorrhage, functional impairment, and spill of tumor tissue This latter danger can be reduced by surrounding the kidney with a surgical pack to catch local spill and by pedicle clamping to avoid hematogenous spread

Pheochromocytoma of the Urinary Bladder—The authors present a 14-year-old boy in whom a diagnosis of leiomyosarcoma of the bladder had previously been made The patient was referred to the authors for probable total cystectomy and ureteroileo-cutaneous urinary diversion Exploration was at first postponed for several days awaiting the original sections, but these did not arrive At operation nodes were found, which suggested metastatic tumor Urinary diversion was necessary to prevent further bleeding from the bladder tumor, and bilateral ureteroileo-cutaneous anastomosis was performed When the original sections arrived, they suggested paraganglioma or pheochromocytoma The possibility of multiple pheochromocytomas was considered in view of the blood pressure response to bladder distention and to manipulation of the tumors at operation Two weeks after diverting the urine, the abdomen was again entered During a dissection of a tumor from the left common iliac artery and vein, the blood pressure remained high Believing that this tumor might represent a 2nd pheochromocytoma, or possibly a metastasis, the bladder, prostate, and seminal vesicles were removed, the blood pressure fell to 120/70 mm Hg and remained there The authors tabulate data on this and 8 other cases of pheochromocytoma of the bladder Six of the 9 patients experienced paroxysmal attacks, which seemed to be brought on by filling or emptying of the bladder All had either paroxysmal or sustained hypertension Six had experienced gross hematuria Surgical excision was carried out in 8 of the 9 patients The ninth patient died in peripheral circulatory failure 48 hours after cystoscopy Seven of the 9 patients are alive, and all but 1 are normotensive

Lancet, London

1 779 834 (April 9) 1960 Partial Index

Reaction to Subcutaneous Drainage in Anasarca
D W Vere and C E King p 779
Multiple Congenital Anomaly Caused by Extra Autosome
K Patau D W Smith and others p 790
Parathyroidectomy in Renal Hyperparathyroidism
S W Stanbury G A Lumb and W F Nicholson p 793

Parathyroidectomy in Renal Hyperparathyroidism—A 33-year-old woman complained of lack of energy and of pain in the shoulders, back, knees and ankles, tracing the onset of symptoms to 9 years previously Polyuria and polydipsia had been present since childhood and the patient s appearance was characteristic of chronic uremia with a sallow complexion and anemia The fecal output of calcium was higher than the dietary intake The ratio of fecal to urinary phosphorus was increased The patient received sodium bicarbonate (4 Gm daily) without results A diagnosis of secondary hyperparathyroidism was established and a parathyroidectomy was performed Five parathyroid glands were identified and a total of 3 50 Gm of parathyoid tissue was removed Hypocalcemia was associated with sensory and motor tetany and a sensation of bodily cold The osseous pain was unchanged Postoperative metabolic studies showed persistent lack of calcium absorption, the clinical picture resembled that of uremic osteomalacia The patient was given 100,000 I U of vitamin D_2 (calciferol) daily, orally, but her condition remained unchanged until the dose of calciferol was increased to 6 25 mg The skeletal pain gradually disappeared, the levels of calcium phosphate, and citrate increased, within 2 months the patient was free of symptoms This patient's hyperparathyroidism was attributed to chronic renal disease, not to a primary parathyroid with secondary renal involvement

Medical Journal of Australia, Sydney

1 641-672 (April 23) 1960 Partial Index

Hypothermia in Cardiac Surgery
B S Clifton p 641
Congenital Facial Diplegia
M Harrison and N Parker p 650
Torsion of Testis Plea for Bilateral Exploration
N Johnson p 653

Congenital Facial Diplegia —This report is concerned with 7 patients who had congenital facial diplegia and who were observed during the past 2 years This indicates that the condition is not as rare as might be deduced from the literature The authors tabulate the clinical feature of these 7 patients Congenital facial diplegia is frequently incomplete, the lower portion of the face is usually less affected than the upper part This distinguishes it from the traumatic group, in which the upper and lower parts are equally involved Four of the 7 patients had bilateral paralysis of the abducens nerve, but this palsy had a distinctive character in that the patients were unable to abduct either eye beyond the mid-line and this was associated with paralysis of conjugate horizontal movement The 12th cranial motor nerve was involved in 3 of the 7 patients Other abnormalities include clubfeet, pectoral-muscle and brachial deformities One of the patients had bilateral talipes equinovarus, another had severe syndactyly, and a 3rd had marked valgus deformities of the distal phalanges of the great toes Two of the 7 patients had mental retardation Immobility of the face, incomplete closure of eyelids when asleep, open mouth, and inability to suck are characteristic The child fails to develop normal speech An investigation of the antenatal histories revealed no evidence of infective, nutritional, or toxic factors A genetic basis is postulated, and evidence is presented in favor of this theory

Minerva medica, Turin

51 1087-1130 (March 31) 1960 Partial Index

Collateral Effects of Streptomycin Therapy in Tuberculosis
A O Zorini p 1087
Secretion of Biliary Acids in External Biliary Fistulas
Q Maggiori and G Vivaldi p 1097
Rare Case of Takayasu Disease
F Marsico and F Coccalatte p 1108

Rare Case of Takayasu Disease —A 33-year-old woman had had, since the age of 11, rheumatic episodes with fever, tonsillitis, Raynaud's phenomenon, intermittent claudication in the upper and lower limbs and in the muscles of mastication, frontal headache, vertigo, and visual disturbances Physical examination revealed absence of pulse on either side, systolic murmur over the right carotid Signs of generalized trophic disorders were manifested in the electrocardiogram The absence of pulse and presence of a carotid murmur indicated complete occlusion of the subclavian and incomplete occlusion of the right carotid The clinical picture was compatible with that of the aortic arch syndrome As negative results of laboratory and roentgenologic examinations eliminated several etiologic factors, it was concluded that the patient had Takayasu's disease, a form of inflammatory, chronic, and obliterating arteriopathy, probably originating in the brachiocephalic arteries The hypothesis that the aortic arch syndrome has an infectious etiology and that the arteritis is the expression of an immunologic reaction of an allergic-hyperergic type is reinforced by the presence of fever, polyarthralgia, and increase in erythrosedimentation

Nederlands tijdschrift v geneeskunde, Amsterdam

104 757-812 (April 16) 1960 Partial Index

Tonsillitis and Peritonsillar Abscess
E Huizinga p 757
Griseofulvin in Treatment of Mycosis
G Cremer p 766
Myeloid Metaplasia and Pheochromocytoma
R Eeckels, C Hooft, and M J Delbeke p 773

Myeloid Metaplasia and Pheochromocytoma —The authors were able to follow up for 5 years the course of agnogenic myeloid metaplasia in a boy who was 2½ years old when 1st admitted to the Children's Clinic of the University of Ghent The boy's weight was below normal and the abdomen was enlarged There was decided splenomegaly, moderate anemia, and severe thrombopenia Examination of the bone marrow revealed the myeloid series to be normal, whereas the erythrocytic series was slightly hypoplastic, there were few and mostly young megakaryocytes After splenectomy the patient's general condition was fair for about 4 years, except that his weight was below normal, and he had hepatomegaly When he was nearly 7 years old he had to be hospitalized again He now presented a number of symptoms indicative of pheochromocytoma He died 5 months later Since both agnogenic myeloid metaplasia and pheochromocytoma are extremely rare in children the authors feel that the simultaneous occurrence can hardly be considered a coincidence They cite experimental studies in which the injection of extracts of the anterior lobe of the hypophysis produced myeloid metaplasia in spleen and adrenals and to a lesser extent in liver and kidneys It was deduced that myeloproliferative processes might be reactions to endogenous, possibly hypophysial, stimulation

New England Journal of Medicine, Boston

262 999-1046 (May 19) 1960

Lung Fibrinolysis in Hyaline-Membrane Disease
J Lieberman and F Kellogg p 999
Repeated Fluoroscopic Examinations on 1480 Children
A McA Birch and D H Baker p 1004
Evaluation of the Heaf Tuberculin Test
A B Robins and J N Daly p 1008
Heart Block (with Stokes-Adams) in Rheumatoid Heart Disease
J D C Gowans p 1012

Lung Fibrinolysis in Hyaline-Membrane Disease —The absence of fibrinolytic enzyme activity in the lungs of newborn infant succumbing to hyaline-membrane disease was demon strated by the inability of lung preparations to activate plasminogen (profibrinolysin) It was postulated that this deficiency and the aspiration of amniotic fluid containing thromboplastin, and an alveolar effusion of blood plasma, as well as air breathing, would complete the development of the hyaline membrane In the absence of fibrinolytic activity the resulting fibrin clot, which would normally be liquefied and removed from the alveolar spaces might be compressed into a hyaline membrane by the respiratory movements of the lungs An improved technique for measuring tissue plasminogen activator activity employs homogenates of lung tissue rather than cubes of whole tissue and results in greater sensitivity of the test The authors used this technique to assay the plasminogen activator activity in lung specimens (obtained at autopsy) of 11 infants with hyaline-membrane formation, 79 adults and children with pulmonary edema, and 46 other infants dying perinatally Nine of the 11 specimens with hyaline-membrane formation completely lacked enzyme activity, and 8 of these specimens also demonstrated an inhibitory effect Two of the 46 control specimens and 7 of the 79 cases with pulmonary edema also lacked plasminogen-activator activity The enzyme deficiency associated with hyaline-membrane disease is thus highly significant and does not appear to be an effect of pulmonary transudation It is thought that the defect in association with an alveolar capillary transudate, predisposes to hyaline membrane formation in the newborn infant and may represent a true genetic deficiency or perhaps enzyme depletion

Evaluation of the Heaf Tuberculin Test—The Heaf test is a multiple puncture tuberculin test developed by Heaf of Wales and used in Britain since 1951 It employs a spring-activated lancet, which causes 6 needles to be driven to a predetermined depth through a drop of tuberculin on the skin The skin of the forearm is cleansed with acetone A drop of a special purified protein derivative (PPD) tuberculin with a concentration of 2 mg per milliliter is applied to the skin This can be done by a flamed inoculating loop, a sterile toothpick or a syringe with 25-gauge needle attached The authors prefer the last method in mass testing They sterilize the apparatus by covering the end plate with alcohol and flaming it The end plate is then applied to the drop of tuberculin and the needles are released The area is allowed to dry, no dressing is used The test is read at 72 hours but can be left for a longer period Four grades of positive reaction are distinguished The Heaf tuberculin test was applied to 61,000 pupils entering 186 New York City high schools during 1958 It was acceptable to both students and staff and was considerably more dependable than the Vollmer patch test Comparative studies with the Mantoux test showed the Heaf test to be highly specific, with a sensitivity level between that of intermediate strength and full-strength tuberculin intradermal tests Heaf reactions can be interpreted with a high degree of consistency, and in certain circumstances may be read by the subjects themselves The Heaf test is a satisfactory substitute for the Mantoux test in mass tuberculin screening programs

Radiology, Syracuse, N Y

74 705 888 (May) 1960 Partial Index

Irradiation of Hemangiopericytoma of Stout
M Friedman and J W Egan p 721
Short Treatment Distance Cesium 137 Teletherapy Unit
A Cole and others p 731
Roentgenographic Aspect of Pulmonary Tularemia
E L Overholt and W D Tigertt p 758
Roentgen Findings in Pseudomembranous Enterocolitis
S B Feinberg p 778
Midgut Volvulus
R P Allen D R Akers and C E Shopfner p 784
Intravenous Cholangiography in Acute Cholecystitis
H C Johnson Jr and others p 790

Irradiation of Hemangiopericytoma of Stout—The authors report on 3 men and 2 women, 27 to 63 years of age, with hemangiopericytoma of Stout, who were treated at the Hospital for Joint Diseases in New York The treatment of this rare tumor is complicated by the diversified clinical picture, the fact that the growth can arise in many parts of the body, including bone as well as connective tissue, and the frequent impossibility of differentiating histologically between benign and malignant forms In these patients the tumor occurred in the right scapula, in the left foot, in the palm of the left hand, in the right calf, and adherent to the dura at the level of the 4th and 5th cervical vertebrae Surgical excision is the treatment of choice, but irradation is frequently indicated because of inoperability or incomplete excision, to avoid amputation, and for palliation in advanced disease Irradiation was performed on all 5 patients The lethal irradiation dose for hemangiopericytoma probably lies in the range of 7,500 to 9,000 rads within 30 to 60 days This high dosage entails a certain risk of radiation injury and can be administered only with some form of supervoltage x-rays or gamma-beam teletherapy Different degrees of palliation can be achieved with smaller doses For minimal palliation as well as symptomatic treatment of widespread disease a minimum tumor dose of 3,000 rads in 18 days is suggested

Roentgenographic Aspect of Pulmonary Tularemia—The authors report serial roentgen findings in 34 laboratory workers in whom pneumonia occurred after accidental respiratory exposure to Pasteurella tularensis Standard 6-foot posterior-anterior and lateral chest roentgenograms were obtained at least twice weekly during the illness and therapy, and thereafter at least every other week until normal conditions were restored Of the 34 patients, 20 had positive roentgenographic findings, pneumonic infiltrates were noted in 17, hilar adenopathy in 9, pleural effusion in 5, and perihilar linear streaking in 11 The pneumonic lesion had a distinctive appearance, in 12 patients there was a single, oval, 2 to 8 cm density with an indistinct border, in 3 there were similar but multiple lesions The inhalation of Past tularensis frequently results in a primary pneumonia This is demonstrable roentgenographically during the 1st week of a grippal illness associated with respiratory symptoms Positive roentgenograms may be obtained as early as the 2nd day of disease, and the lesions may be single or multiple There is often an associated hilar adenopathy with or without pleural effusion The combination of ovoid pulmonary infiltrates and hilar adenopathy should prompt the consideration of respiratory tularemia

Intravenous Cholangiography in Acute Cholecystitis—The authors report on 220 patients with acute abdominal signs and symptoms suggesting acute cholecystitis who were subjected to emergency cholangiography by means of intravenous administration of iodipamide (Cholografin) at Grady Memorial Hospital, Atlanta, Ga In 69 of the 220 patients subsequent data confirmed the diagnosis of acute cholecystitis The procedure proved a reliable, rapid, and safe method of establishing the presence or absence of obstruction of the cystic duct On this basis a suspected clinical diagnosis of acute cholecystitis could be confirmed or excluded False positive and false negative cholangiographic diagnoses of acute cholecystitis were not made provided that a diagnosis of obstruction of the cystic duct was deferred until a 4-hour roentgenogram of good quality has been viewed Studies of the hepatic uptake of radioactive iodipamide frequently showed impaired liver function in the acutely ill patient This procedure may prove useful in selecting patients suitable for emergency cholangiography by means of intravenous administration of iodipamide

Settimana medica, Florence

48 155-174 (March 15) 1960

Lysergic Derivative in Migraine and Epilepsy
F Sicuteri p 155
Status of Therapy in Tuberculous Meningitis
G Invernizzi G Vailati, and P L Gerali p 162
Antitetanic Prophylaxis Social and Medicolegal Aspects
N Gennai p 168

Status of Therapy in Tuberculous Meningitis—Three groups of patients were treated by different methods The 55 patients in group 1 (1947-1952) received injections of streptomycin Sixteen of them recovered without sequelae, 22 recovered with sequelae, and 33 died In group 2 (1952-1959), 34 patients received injections of streptomycin plus isoniazid given orally Twenty-five patients recovered without sequelae, 2 had sequelae, 7 died In group 3 (1956-1959), 11 patients were treated as in group 2 with the addition of cortisone or hydrocortisone injected into the spinal canal Seven patients recovered without sequelae and 4 died In groups 2 and 3, 1 Gm of streptomycin was given daily for 40 days, then in 10-day series for 5 or 6 months Isoniazid was given in the dosage of 6 mg per kilogram of body weight for 4 months, then in 10-day series alternating with streptomycin From the 6th to the 7th month 20-day series of isoniazid were alternated with 10-day series of streptomycin Patients with spinal block (group 3) received an intraspinal injection of 8 cc of streptomycin sulfate plus 10 mg of hydrocortisone or cortisone for 4 or 5 consecutive days, then every other day for 20 days, then twice a week, and finally once a week until normalization of the spinal fluid was achieved Adjuvant therapy with vitamins, calcium, and liver extract was given to all patients The increase in the over-all rate of cure (40% in group 1, 79 42% in group 2, and 63 64% in group 3) is attributed to the isoniazid-streptomycin combination and to the intraspinal administration of cortisone or hydrocortisone The importance of early diagnosis and treatment is emphasized

Surgery, Gynecology & Obstetrics, Chicago

110 519-646 (May) 1960 Partial Index

Excretion of Calcium and Phosphorus After Surgery
K N Wynne, S H Chorlton, and K W Starr p 519
A Three Year Study of Staphylococcal Disease
H Taylor Caswell and others p 527
Coagulation Changes in Experimental Phlebothrombosis
H M Mann and others p 541
Preinvasive Intraductal Carcinoma of Breast
D A Gillis, M B Dockerty, and O T Clagett p 555
Management of Lesions of Ureter with Fistula
S R Weinberg, F C Hamm, and B Berman p 575
Lung Biopsy
T W Shields and S K Sweany p 585
Basic Surgical Principles of Ureteral Repair
R G Weaver p 594
Fat and Nitrogen Metabolism After Gastrectomy
W Lawrence Jr and others p 601

Preinvasive Intraductal Carcinoma of the Breast—Carcinomas of the breast originate in ductal epithelium or its derivatives The pathologist, however, will see epithelial alterations within ducts that must be regarded as neoplastic in nature but in which the cells have not acquired the aggressive, anaplastic, and infiltrative characteristics of mammary carcinoma In order to define the preinvasive intraductal carcinoma more clearly, the authors reviewed 603 surgically excised lesions of the breast diagnosed as comedocarcinoma Tumors associated with Paget's disease (of nipple) and those which on preliminary review exhibited even minor degrees of stromal infiltration were eliminated The 50 remaining lesions were scrutinized again, many new blocks were cut, and 14 lesions were found to be invasive on second appraisal Further studies were made on 36 cases of what might be called in situ carcinoma of the breast. This variety of breast tumor does not produce any characteristic symptoms, and the classic clinical signs of malignancy are usually absent The major change is ductal dilatation, with or without visible intraductal plugs of tumor The identification of this entity requires thorough microscopic study of the involved tissue The surgical pathologist cannot be expected to state that a given tumor is entirely intraductal only on the basis of preliminary review of frozen sections Therefore, the surgeon should not base his decision for or against radical surgery on the results of this examination Carcinoma of the breast does not involve the regional lymph nodes as long as it is still confined to the ducts The life expectancy of patients from whom a preinvasive intraductal carcinoma of the breast has been removed is not altered by the disease

Fat and Nitrogen Metabolism After Gastrectomy—A total of 103 metabolic balance studies were carried out on 42 patients in a metabolic unit Diets were homogenized, and were analyzed for fat and nitrogen A 3-day adjustment period, on an identical diet, was followed by 3-day metabolic balance periods Mean fat absorption after total gastrectomy was 81 7% of intake (normal range, 92 to 100%), but there was much variation between patients The percentage of absorption of dietary fat in individual patients was unaffected by variations in fat intake, it was generally decreased by increasing dietary carbohydrate and was usually increased when hydrochloric acid was administered Protein absorption was also decreased after total gastrectomy By increasing the dietary carbohydrate, nitrogen absorption was reduced, but total retention of nitrogen was slightly increased as judged by urinary nitrogen measurements Hydrochloric acid supplements decreased protein absorption slightly but did not cause a negative nitrogen balance Comparing the mean dietary protein intake required to achieve zero balance after total gastrectomy with similar calculations from groups of normal subjects demonstrated a definite increase in dietary nitrogen requirement in these patients Metabolic studies after subtotal gastrectomy showed similar, but less striking, variations in both fat and nitrogen metabolism Comparison of metabolic data with body weight studies in the same patients showed a poor correlation between the nutritional state and the absorption defects The most important factor in nutritional maintenance seemed to be the ability to control postprandial symptoms sufficiently to allow adequate intake With careful dietary management the majority of patients could be maintained in an adequate nutritional state, and this fact seems to justify total gastrectomy for cancer of the stomach

WASHINGTON NEWS

Aged Health Bill Sessions
Social Security For Physicians
Arthritis Cure Claims Challenged
New Drug Law
Miscellany

FINANCE COMMITTEE TAKES UP HEALTH BILL

The Senate Finance Committee launched closed-door hearings on health care for the aged legislation, and Committee Chairman Harry F Byrd (D, Va) issued a warning to Democrats backing Social Security health programs

The Virginia lawmaker said the committee might be forced to hold time-consuming public hearings if liberals press demands for legislation extending medical benefits as part of Social Security Open sessions would not be necessary if the Finance Committee adopts the House-approved bill calling for a voluntary, federal-state plan of helping medically indigent persons to finance their health care, according to Sen Byrd

It was expected that the Finance Committee would consider the health care measure for at least a week, and possibly longer The health care provision of the House bill is only part of a catchall measure containing various changes in the Social Security program, including liberalization of the program for permanent and totally disabled persons and bringing physicians under social security for the first time

Meanwhile, both Democratic and Republican leaders placed 'must' labels on health care legislation President Eisenhower submitted a 22 point program for congressional action at the bob-tail session that included assistance to older people to meet serious illnesses Vice-president Richard M Nixon and Senate Republican Leader Everett M Dirksen (Ill) listed as among five 'must issues medical care for the aged Senate Democratic Leader Lyndon Johnson (Texas) predicted that Congress will pass a medical care bill this session One already would have cleared Congress, he said, except that the Administration 'couldn t make up its mind whether it wanted a bill or not, and when it did, what kind it wanted

The priority tags placed on the legislation did not necessarily assure Congressional passage

Here are some of the things that could happen in Congress

1 The Senate might become embroiled in other controversial issues and not have time to act on the legislation this year

2 The Senate could approve the House-passed bill and send it to President Eisenhower The Administration has endorsed the principle of the House measure

3 The Senate could tack on a Social Security health program This would require sending the entire issue back to the House of Representatives There, a stalemate between the two chambers could develop that could result in no final congressional action this year Another possibility is the development of a compromise bill Or,

4 The House could accept a Senate Social Security health plan Even this eventually would not necessarily end the matter President Eisenhower has repeatedly asserted his all-out opposition to any compulsory health program Odds are against any overriding of a Presidential veto

The American Medical Association urged rejection of the Social Security approach and approval of the House-passed voluntary plan in a full-page statement placed in some large metropolitan daily newspapers In the statement signed by the officers and trustees of the Association, the AMA said it 'enthusiastically endorses the principle of helping those among the aging who need help

We are equally sincere in our opposition to legislative measures that approach the problem on a shotgun basis—with the idea of increasing repeatedly the social security tax in order to finance health benefits for EVERYONE who is covered by the Old Age, Survivors, and Disability Insurance program, regardless of the individual's need

There are many serious hazards in using the Social Security approach to finance medical and hospital care for our older citizens When government starts telling the doctor how to practice medicine, telling the nurses how to nurse, telling the hospital how to handle its patients—the quality of medical care is sure to decline The cost of such a program eventually would be staggering, and would make a serious dent in the pay envelopes of millions of Americans covered by social security Private voluntary health insurance, which has been doing such a magnificent job, would be undermined and, in time, destroyed

'Most important, perhaps, is the fact that such an approach would be just the beginning of compulsory, government-run medical care for every man, woman and child in the United States For it wouldn t be long before the federal government would be lowering the age at which people would be eligible, and adding one costly service after another to a program that would place your health care under the federal government s thumb And let s not forget that our present health care is recognized to be the world s finest

(Continued on next page)

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brand Erythrol Tetranitrate

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'Cardilate' provides, in one drug, rapid onset of effect (5-10 minutes) and prolonged duration of vasodilating action (4-5 hours), thereby facilitating adjustment of the therapeutic regimen to the angina patient's daily activities For those whose plans vary from day to day, the rapid effect of Cardilate' permits administration of the drug just prior to known angina-precipitating situations.

For a routine day, the following schedule of administration is suggested

Time	On arising	At lunchtime	4 to 5 P.M.	At bedtime (P R.N)
Dose	5 15 mg	5 15 mg	5 15 mg	5 15 mg

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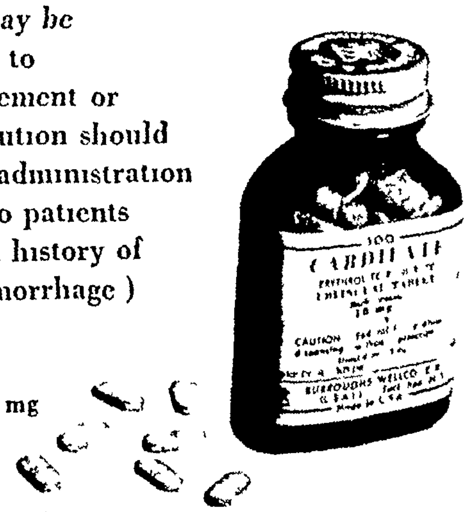

15 mg.

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COMMITTEE REJECTS SOCIAL SECURITY FOR PHYSICIANS

The Senate Finance Committee tentatively voted to knock out of a House-passed Social Security measure a provision bringing self-employed physicians under the Social Security system for the first time The vote was 11 to 4

Committee Chairman Harry F Byrd (D, Va) said the decision was made because the American Medical Association had requested the action

The House Ways and Means Committee had voted to bring physicians under the program despite the protests of the A M A that a majority of physicians were opposed to being in the program The Administration had requested that self-employed physicians be brought into the system

At the A M A's annual convention in Miami Beach, Fla , in June, the House of Delegates unanimously reaffirmed the A M A's position against Social Security coverage for physicians

FTC ISSUES ORDER AGAINST ARTHRITIS BOOK

The Federal Trade Commission moved against a second best-selling book claiming to offer valid health advice The latest book was "Arthritis and Common Sense," by Don Dale Alexander, a book which has sold more than 500,000 copies

The FTC ordered the book's publishers to halt allegedly false claims that the diet recommended in the book would cure arthritis and rheumatism The previous week, the agency issued a similar order to publishers of the book, "Folk Medicine, also purchased by some 500,000 readers

In issuing the order against "Arthritis and Common Sense," the FTC upheld an examiner's finding that "there is no creditable or other testimony or facts on record, worthy of consideration or belief, in substantiation of the theories of the book " The book states that arthritis and related conditions will be corrected and effectively relieved by a dietary regimen which includes cod liver oil and orange juice and use of other foods and beverages prepared and eaten in sequences recommended

The Arthritis and Rheumatism Foundation said it "has always viewed the wide circulation of these theories as a grave menace to arthritis sufferers It is a medical fact, which the foundation has always stressed, that diet can neither cause nor cure arthritis "

DRUG LEGISLATION SIGNED

The Federal Narcotics Bureau was armed with new weapons against drug addiction as a result of legislation recently signed into law by President Eisenhower

The bill gives the Federal Narcotics Commissioner broader leeway in placing or lifting government controls on drug preparations with small amounts of narcotics, and new supervisory powers over basic classes of narcotics

One of the major reasons for the new law was reports of youth becoming addicted to preparations containing small amounts of narcotics and requiring no physician's prescription One such preparation, according to a bureau spokesman is dihydrocodeinone, a cough syrup

The legislation also authorizes the Narcotics Bureau to set quotas on the amount of narcotics individual manufacturers can produce The quotas would be based on estimated medical and scientific needs of the nation The government was empowered to license narcotics drug producers for the first time

The law goes into effect the first of the year

MISCELLANY

The U S Public Health Service approved 66 grants totaling $21 9 million to help build and equip additional health research facilities in 55 institutions across the country Largest grant, $1 8 million, went to Memorial Center for Cancer and Allied Diseases, New York, for research laboratories in New Memorial Center Building Grants of more than $1 million were awarded State University of New York's Upstate Medical Center, Medical College of Virginia, Richmond, University of Colorado, Harvard University, and University of Mississippi

The Agriculture Department reported the possibility that a form of poultry cancer, long considered to be non contagious, can be transmitted by contact 'Overwhelming evidence has come out of two trials at the Agriculture Department Poultry Laboratory at East Lansing, Mich, showing that the virus of Rous sarcoma was transmitted to healthy chickens raised in direct contact with birds inoculated with the virus," said the Department

The Civil Service Commission said about 1,450,000 government employees had signed up through mid-July in contributory health insurance programs under the new program authorizing federal contributions for U S workers health insurance Some 56 per cent were registered with Blue Cross-Blue Shield, a government-wide indemnity plan underwritten by Aetna Life Insurance Co accounted for 27 per cent, employe organization plans, 11 per cent, and direct service plans, 6 per cent

Congress gave Veterans Administration appropriations for medical purposes another boost this year Appropriations for fiscal 1961, which started July 1, as compared to last year are as follows Inpatient care in VA hospitals—$817 million and $742 8 million, outpatient care—$86 5 million and $83 9 million, and medical research—$21 5 million and $18 3 million

Americans were urged to line up 100 per cent behind the drive for polio vaccinations U S Surgeon General Leroy Burney said most of the 310 cases reported so far this year could have been prevented if the individuals had taken the required number of inoculations Although less than half as many cases have been reported so far this year as the same time last year, the dangerous period lies ahead," said Dr Burney It is by no means too late to start vaccinations The goal should be no less than 100 per cent immunization

The Justice Department was asked by the Department of Health, Education and Welfare to bring suit against the city of St Joseph, Mo, to force the city to eliminate pollution in the Missouri River A bond issue which would have allowed the city to build sewage facilities to handle the problem failed to win approval in St Joseph last May The legal action was the first taken under a new law giving the federal government power to take action against municipalities that do not clean up pollution on interstate waterways

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brand Erythrol Tetranitrate
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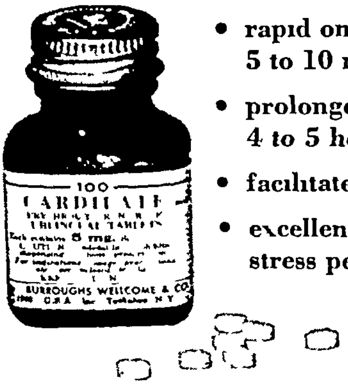

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Riseman, J E F, *et al* Circulation 17 22 (Jan) 1958

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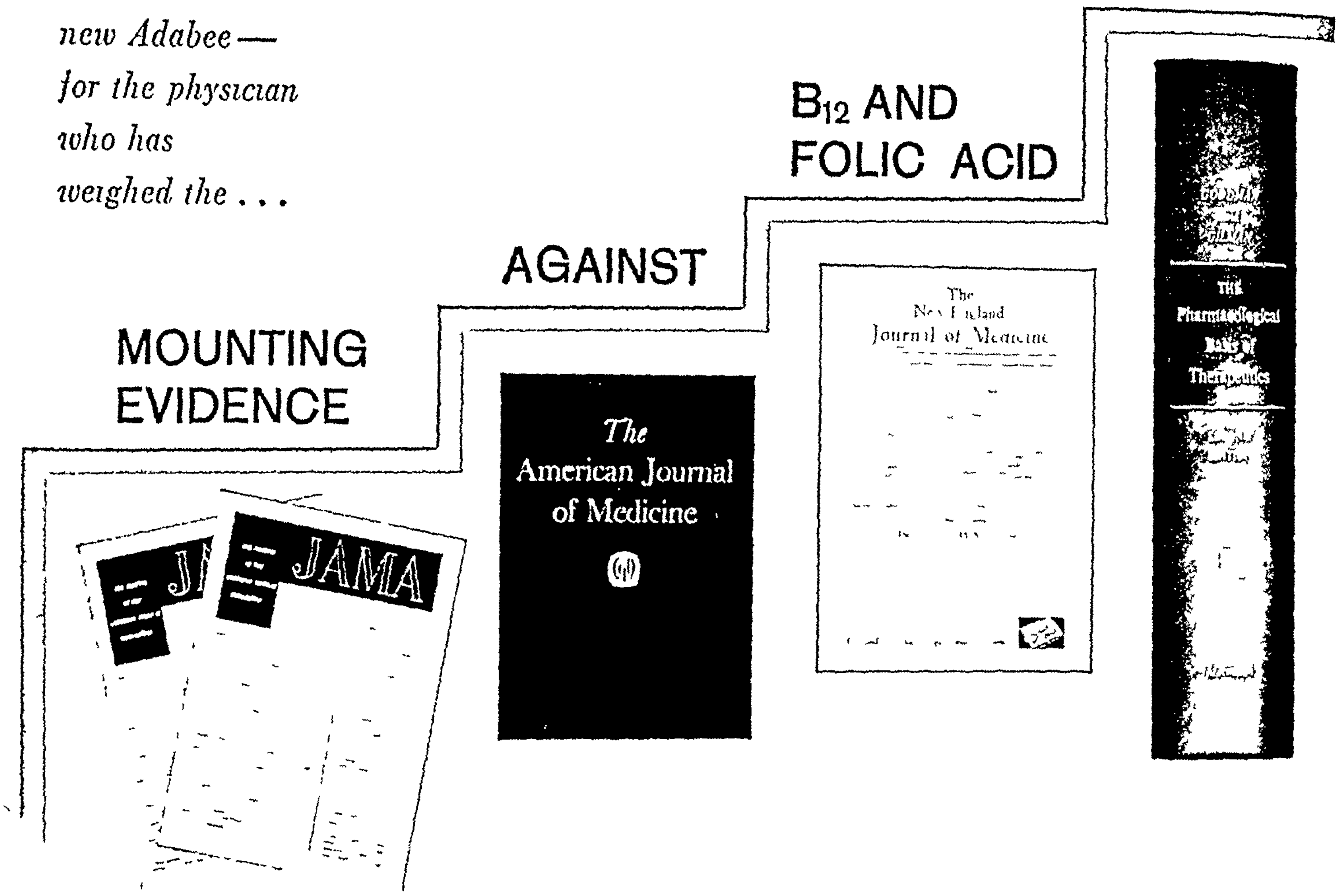
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The American Journal of Medicine
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Individually, folic acid and vitamin B$_{12}$ fill important clinical roles[1] But, increasing evidence indicates that multivitamins containing folic acid may obscure the diagnosis of pernicious anemia[2-7] And vitamin B$_{12}$, in indiscriminate and unnecessary usage[5-8] is likewise linked to this diagnostic confusion[7]

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references: 1 Wintrobe, M M, *Clinical Hematology,* 3rd ed, Phila, Lea & Febiger, 1952, p 398 2 Goodman, L S and Gilman, A, *The Pharmacological Basis of Therapeutics,* 2nd ed, New York, Macmillan, 1955, p 1709 3 New Eng J M, Vol. 259, No. 25, Dec 18, 1958, p. 1231 4 Frohlich, E. D., New Eng J M, 259 1221, 1958 5 J A M A, 169 41, 1959 6 J A M A, 173 240, 1960. 7. Goldsmith, G A, American J of M, 25.680, 1958 8 Darby, W J, American J. of M, 25 726, 1958.

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ETIOLOGICAL FACTORS IN DIABETIC NEPHROPATHY

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and
M S Sabour, D M , M R C P , Grimsby, England

Factors that might affect the development of diabetic nephropathy were sought in a study of 391 patients with diabetes mellitus "Diabetic proteinuria" was found in 47 No sex difference in incidence was noted but in males, the frequency of its occurrence was greatest in the higher age group, while in females there was no statistically significant difference in distribution among various age groups The frequency of proteinuria increased greatly with increase in the duration of diabetes No correlation was found between diabetic proteinuria and the severity of diabetes as rated by the fasting blood sugar level It was confirmed that the development of proteinuria in the diabetic is very much related to the degree of control of the diabetic state The biophysical and biochemical abnormalities which result from poor control are suggested as factors in the pathogenesis of the nephropathy

THE introduction of insulin and of antibiotics has saved the diabetic patient from early death from coma and infections and has increased the life expectancy about threefold, but at the same time degenerative diabetic lesions have become more and more frequent and are now the chief problem in this disease Among these, diabetic nephropathy stands as the most important, and White[1] considered it as the cause of death in 51% of her diabetic patients

Although much has been done to elucidate the various factors which are responsible for the development of nephropathy in the diabetic subject, a wide divergence of opinion still exists All authors agree only that diabetic nephropathy is related to the duration of the diabetic state, but wide variation occurs in relation to the other etiological factors Thus Mann and colleagues[2] noted that diabetic nephropathy occurs more frequently in patients with severe diabetes, while Zubrod and co-workers[3] suggested that a specific or unique type of diabetes characterized by mild severity and no, or very infrequent, episodes of acidosis is associated with diabetic nephropathy, still others believe that there is no correlation between diabetic nephropathy and the severity of diabetes The effect of age and sex on the development of nephropathy is not universal The main point of controversy is whether good control of the diabetic state over the years protects the patient from the degenerative complications or whether they are a part of the natural history of the disease, and will develop if the patient lives long enough for them to appear

Realizing all the previous work in this field we attempted to restudy the factors which bear on the development of diabetic nephropathy Three hundred ninety-one patients attending the diabetic clinic in Ain-Shams University Hospital, Cairo, were chosen for study, without any specification, from both sexes and all ages There were 192 male

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From the Department of General Medicine and the Renal and Diabetic Clinics Faculty of Medicine Ain Shams University Cairo U A R and 199 female subjects The youngest was a 6-year-old boy and the oldest an 80-year-old woman The age distribution of these patients is noted in figure 1

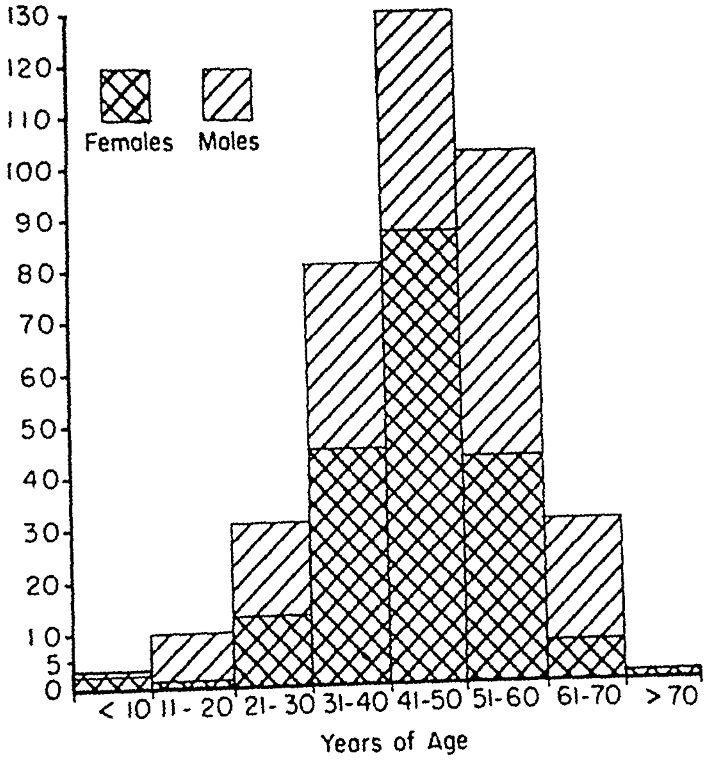

Fig 1 —Age group of patients under discussion

The patients chosen for the analysis were those attending the clinic for a minimum of five years It is the rule in the clinic to analyze urine for protein, sugar, and acetone content on each occasion the patient attends, which, on the average, is bimonthly once his diabetes is considered controlled Fasting blood sugar estimations are made at six-month intervals on every patient attending the clinic Thus, during the five-year minimum follow-up period of the patients included in this study, a minimum of 10 fasting blood sugar estimations were made It is on the basis of the results of these urine and blood analyses that the patients were classified for the study

Table 1 —*Frequency of Proteinuria in Diabetics in Various Age Groups*

	Male			Female		
		Diabetic Proteinuria			Diabetic Proteinuria	
Age, Yr	No of Patients	No	%	No of Patients	No	%
< 10	1			2		
11 20	9			1		
21 30	18	1	5 5	13	1	7 8
31-40	36	2	5 5	45	7	15 5
41 50	43	5	11 [illegible]	87	9	10 4
51-60	61	7	11 0	42	5	11 4
61 70	24	8	33 3	7	2	18 5
> 70				1		
Total	192	23	12 5	199	24	12

Pertinent Findings

Frequency of Proteinuria —Protein in the urine was detected by the heat coagulation test, microscopic examination of the urinary sediment was always done if proteinuria was found The patients with proteinuria could be divided into two groups (1) those with a coincidental and most often transient proteinuria from affections not directly attributable to the underlying diabetes such as (*a*) postrenal affections, prostate, calculi, cystitis, pyelitis, and bilharziasis or (*b*) renal proteinuria due to a predisposing factor other than the diabetes itself, such as abscess, carbuncle, or gangrene, and (2) those with persistent proteinuria (and casts) as an indication of renal damage, when there was no apparent cause other than the diabetes itself This is referred to as "diabetic proteinuria"

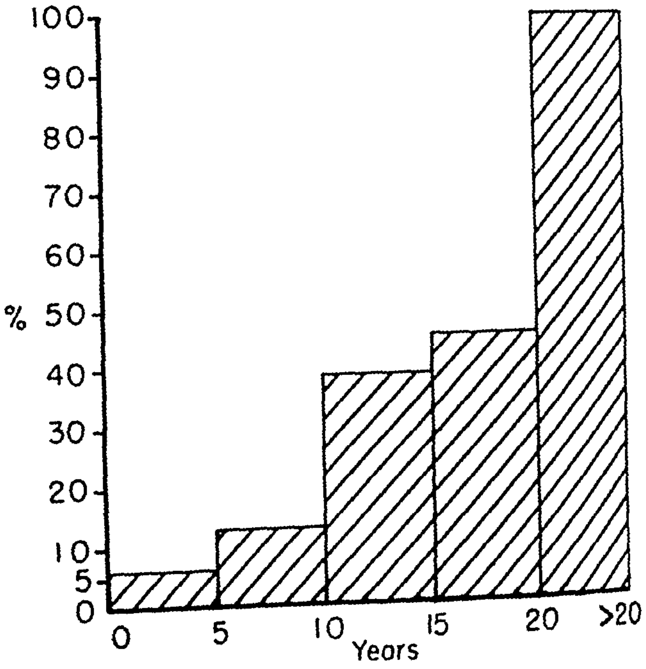

Fig 2 —Relationship between duration of diabetes and proteinuria

Diabetic proteinuria was found in 47 patients, or 12%, 23 male (12 5% of the total) and 24 female (12% of the total) patients It was not found in persons under 20 years of age Table 1 shows the frequency of its occurrence in the various age groups In male patients the frequency of occurrence is greatest in the older age group The difference between the various age groups is statistically significant in male patients In female patients diabetic proteinuria is relatively evenly distributed among the various age groups, with no statistically significant difference

Relation of Diabetic Proteinuria to Duration of Diabetes —Figure 2 shows the percentage frequency of diabetic proteinuria in this series in both sexes, with a duration of 0 to 5, 5 to 10, 10 to 15, 15 to 20, and over 20 years from the time the diabetes was first diagnosed It can be seen that the frequency of proteinuria increases greatly with increase in the duration of diabetes While only 6% of those who have had diabetes for 0 to 5 years have proteinuria, the corresponding figure for those who have had it for 5 to 10 years is 12 8%, for 10 to 15 years 39 1%, for 15 to 20 years 45 5%, and for more than 20 years 100%, (table 2)

TABLE 2—*Relationship Between Duration of Diabetes and Proteinuria*

	Patients		
		With Diabetic Proteinuria	
Duration Yr	No	No	%
0-5	261	16	6 0
5-10	86	11	12 8
10-15	29	11	39 1
15-20	11	5	45 4
>20	4	4	100 0
Total	391	47	12 0

In order to find out whether there was any demonstrable difference between those developing diabetes at an early age and those developing it later in life, the series of male and female patients were divided into two groups, depending on whether diabetes developed before or after the age of 40 years One hundred ninety-nine patients developed it before and 192 after 40 In those developing it after 40, 11 had proteinuria 0 to 5 years later (5 7%), while the corresponding number for those developing diabetes before 40 years of age is five (2 5%) Thus, it appears that diabetic proteinuria develops more readily in older patients, as might be expected in view of the increasing liability to degenerative vascular affections with increasing age

To obviate the factor of age in the study of the effect of duration on the incidence of diabetic proteinuria, the age group 41 to 50, which comprised the largest number of patients, was chosen This age group comprised 130 patients, male and female The incidence of diabetic proteinuria is seen in table 3, the results in which are similar to those of the whole group of diabetics, indicating that it is not the age of the patient but the duration of the diabetic state that is important in the occurrence of diabetic proteinuria The single patient with diabetes of 20 years duration who did not show proteinuria is significant, as her disease was perfectly controlled

TABLE 3—*Relationship Between Duration of Diabetes and Proteinuria in Patients Between Forty-one and Fifty Years of Age*

	Patients		
		With Diabetic Proteinuria	
Duration Yr	No	No	%
0-5	84	6	7
5-10	35	5	14
10-15	10	5	50
15-20	1		0
Total	130	16	13

Relation of Diabetic Proteinuria to Severity of Diabetes—The severity of the diabetic state was divided into three grades according to the fasting blood sugar (F B S) level and the dose of insulin required to control the glycosuria, with the blood sugar estimated by the Folin-Wu "venous' method The three grades were as follows Grade I FBS level below 200 mg per 100 ml and insulin not more than 20 units, Grade II FBS level between 200 and 400 mg per 100 ml and/or insulin between 20 and 40 units and, Grade III FBS level above 400 mg per 100 ml and/or insulin more than 40 units per day Of the 391 patients, 106 were classified as Grade I, 171 as Grade II, and 114 as Grade III Table 4 shows the percentage frequency of diabetic proteinuria in the three grades of diabetics There is no correlation between diabetic proteinuria and the severity of diabetes, it occurs in the same frequency in patients with mild, moderately severe, and severe diabetes

TABLE 4—*Relationship Between Severity of Diabetes and Diabetic Proteinuria*

	Patients		
		With Diabetic Proteinuria	
Grade	No	No	%
I	106	14	13 2
II	171	19	11 1
III	114	14	12 3
Total	391	47	12 0

TABLE 5—*Relationship Between Control of Diabetes and Incidence of Diabetic Proteinuria*

	Patients		
		With Diabetic Proteinuria	
Control Rating	No	No	%
0	25		
½	9		
1	83	2	2 4
2	86	2	2.3
3	89	13	14 6
4	100	30	30 0
Total	391	47	12 0

Relation of Diabetic Proteinuria to Control of Diabetes—In considering the degree of control of diabetes, the grading used by Hardin and colleagues was adopted, in which the following grades were used "0" indicates freedom from sugar in the urine except for occasional slight traces, with approximately normal blood sugar level "excellent", ½" shows fluctuation from rating 0 to rating 1, 1" indicates that less than half the urine specimens are free from sugar, with a small amount of sugar in the remainder and slightly elevated blood sugar levels— fair", "2" shows fluctuation from 1 to 3, 3" indicates constant glycosuria and elevated blood sugar levels—"poor", and "4" shows continuous gross glycosuria and elevated blood sugar levels— 'very poor.' The number of patients in each group is seen in table 5. The number with diabetic proteinuria was determined. From this table and from figure 3 it can be easily seen that the development of proteinuria in the diabetic is very much related to the degree of diabetic control. Thus, the duration of the diabetic state and the degree of control are the factors that produce the renal lesions and not the severity of diabetes.

It is now essential to determine whether the long duration of diabetes per se will produce proteinuria in the presence of excellent control and the duration will be the sole factor and the nephropathy considered as a natural sequel of long-standing diabetes, or whether the long duration produces its effect through prolonging the lack or deficiency in control.

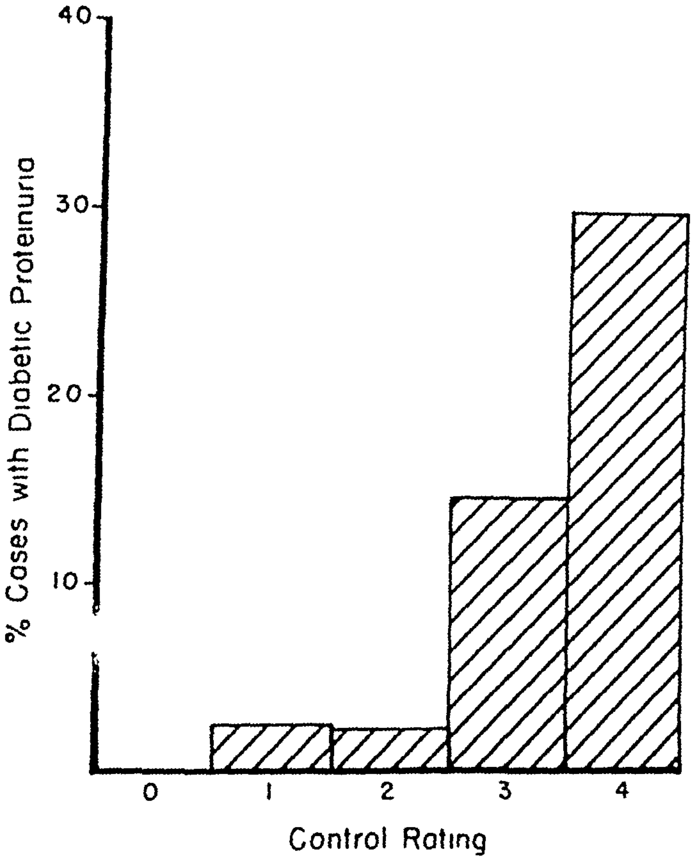

Fig 3.—Incidence of diabetic proteinuria according to control of diabetes.

One patient had diabetes for 20 years, one patient had it for 12 years, one patient had it for 11 years, and three had it for 10 years each, but all had an excellent "0" degree of control and did not show any proteinuria, while many patients with diabetes of less than five years' duration, but all with Grade III or IV control, showed proteinuria.

To illustrate the combined effect of the degree of control and the duration of the diabetic state, the figure for the control rating was multiplied by the duration of the diabetic state in years. Table 6 and figure 4 illustrate the relationship between diabetic proteinuria and this "overall-control rating." It will be obvious that patients showing figures above 50 in the over-all control rating all had diabetic proteinuria.

TABLE 6.—*Incidence of Diabetic Proteinuria According to Over-all Control Rating*

	Patients	With Diabetic Proteinuria	
Over-all Control Rating	No.	No.	%
0-10	248	7	2.8
11-20	76	8	10.5
21-30	29	7	24.1
31-40	10	7	38.8
41-50	7	5	71.4
51-60	6	6	100.0
61-70	1	1	100.0
71-80	3	3	100.0
81-90	1	1	100.0
91-100	2	2	100.0

Comment

Incidence of Diabetes According to Sex and Age.—A slightly higher incidence of glomerulosclerosis in female diabetics has been noted in most references.' The results of most authors show quite a good agreement that the incidence ratio of the histological lesions in female to that in male patients varies between 1.2 and 1.75 to 1, with an average of 1.5. The results of Horn and Semetana, whose results in other respects are completely at variance with the rest of the literature, are the exception.

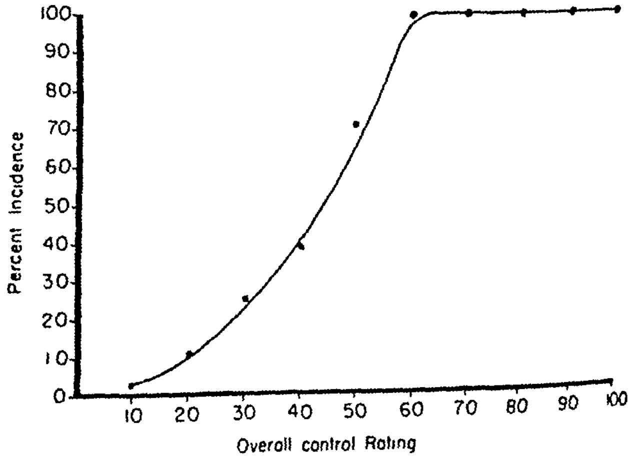

Fig 4.—Incidence of diabetic proteinuria according to over-all control rating.

In this series, diabetic proteinuria was found in 12.5% of male and in 12% of female subjects. Bjerkelund[6] found diabetic proteinuria in 9% of male and 12% of female patients. Mann and colleagues[2] recorded the lesion in twice as many male as female subjects, and Zins[7] says that no preponderance of the lesion will exist in either sex

Thus, it appears that sex does not particularly influence the incidence of diabetic nephropathy

In male patients, as shown above (table 1), the frequency of occurrence is greatest in the older age group, while in female patients diabetic proteinuria is relatively evenly distributed among the various age groups Bjerkelund [6] arrived at this same result It is possible that testosterone inhibits to some degree the development of diabetic nephropathy, and after the male climacteric a sharp rise in the incidence results, while the menopause has no effect on the incidence in females This hypothesis can be accepted with the theory of pituitary-suprarenal cortical hyperfunction, incriminated in the pathogenesis of diabetic nephropathy [8]

Diabetic nephropathy is rare in patients under the age of 30 years In this series it was not found in persons under 20 years of age In the literature only four autopsy cases of glomerulosclerosis are recorded in persons aged under 20 Laipply, Eitzen and Dutra [5d] reported on a patient aged 16 years, Goodof [5e] reported on two patients, aged 17 and aged 19 years, and Henderson, Sprague, and Wagener [5f] reported on one patient aged 18 years The part played by the duration of diabetes must be remembered The increased survival rate of diabetic children in recent years is probably altering the age distribution of diabetic nephropathy, and many patients under 40 years of age are found in the recent as compared with the older reports

Duration of Diabetes—There is sufficient evidence in the literature, in addition to the present findings, to indicate that the presence and sometimes the severity of diabetic nephropathy is definitely related to the duration of the diabetic state [9] As shown above, the older the patient the shorter the duration of the diabetes necessary for him to develop diabetic nephropathy, the duration is thus an important causal factor in the production of the lesion, particularly in the younger age group

Severity of Diabetes—The findings in this study have shown no correlation between the severity of diabetes and the development of nephropathy Diabetic acidosis occurred at least once in 21 of the 47 patients with diabetic proteinuria The results do not indicate that there is a specific type of diabetes associated with diabetic renal disease

Control of Diabetes—When the degenerative lesions which occurred with long-standing diabetes have become so prominent, the question is asked whether these lesions are a part of its natural history or whether they are complications If the first viewpoint is proved to be correct, the diabetic patients must be regarded as facing the inexorable cause of an unalterable disease Contrariwise, if the other concept is the true one, degenerations should be preventable, when the pathologic physiology of their production is understood

Reports of investigators offer varying conclusions A series of papers from the Joslin Clinic emphasize that good control is of utmost importance in the prevention of degenerative vascular lesions Others [10] hold the same opinion The opposite view has also been presented by many reports, such as those of Dolger,[9a] Larsson, and others,[11] McNeal and Rogers,[9b] and others In this study, a definite relationship between the degree of control of diabetes and the incidence of diabetic nephropathy was found The incidence of nephropathy was directly proportional to the interval-control rating and particularly to the over-all-control rating All patients with over-all-control ratings above 50 showed diabetic nephropathy (also retinopathy and neuropathy) It is apparent that a shorter duration, e g, 5 years, is sufficient for a poorly controlled diabetic to develop these complications, while a longer time, e g, 10 or 15 years, is necessary for a moderately controlled diabetic to develop them, and a patient with an excellent degree of control of his metabolic error will not develop vascular complications no matter how long his diabetes remains The duration of diabetes thus plays its role only in the presence of deficient control by prolonging the period of this deficient control and exaggerating an abnormal physiology in the poorly controlled diabetic subject

Biochemical and biophysical abnormalities resulting from poor control of the disturbed carbohydrate and lipid metabolism should be sought Lack of control apparently exaggerates the basic differences and abnormalities in the physiology of diabetes and in this way is responsible for the development of the vascular complications In this connection, we have found [8] that the urinary levels of 17-hydroxycorticosteroids are high in diabetics with ketosis and return to normal after control of the ketosis The 17-ketosteroid levels are low during ketosis and also return to normal values after control High 17-hydroxycorticosteroid and low 17-ketosteroid levels are constant features of diabetic nephropathy [8] Thus, uncontrolled diabetes in some way stimulates adrenocortical activity Considering this with the theory of supraprenal-cortical hyperfunction as a pathogenic factor for the development of the degenerative complications of diabetes, a link is easily drawn explaining the mechanism, or at least one of the mechanisms, of how uncontrolled diabetes accentuates vascular degeneration This observation parallels the experimental finding of Field,[12] that regulation of alloxan diabetes in rats with insulin during 72 hours prevented the occurrence of adrenal hypertrophy in the treated animals

This should open a field of study to compare the various endocrine and metabolic aspects in well-controlled diabetics and in diabetics with ketosis and to correlate any findings with the well-known hormonal and metabolic differences between noncomplicated diabetics and diabetics with degenerative complications Schneider and colleagues[13] noted a low serum albumin level and a high beta globulin fraction in diabetics, especially those with diabetic retinitis Similar changes were found in uncontrolled diabetics While the changes in patients with retinitis did not respond to control of diabetes, those in uncontrolled diabetics returned to normal values with control Lack of control of diabetes, thus, produces a metabolic disturbance which, when it lasts for a long time, will be irreversible and probably responsible for the development of the vascular degenerative lesions

Dolger, Lichtenstein, and Tolstoi, who regard premature vascular disease in the diabetic as inevitable because of the duration of the disease, have advocated a "free diet" and insulin given only to the extent of preventing acidosis and actual symptoms Dunlop,[5c] Wilson and co-workers,[9c] White,[1] and others, who believe that these complications are the result of uncontrolled diabetes, stress a consistent and vigorous treatment designed to provide an adequate diet and at the same time to control the hyperglycemia, the glycosuria, and the hypercholesteremia We believe that the discovery of the various factors that have a role in the pathogenesis of these complications, such as a rise in the serum polysaccharide levels, a rise in the serum lipoprotein aggregates of Svedberg flotation units (S_f) 12-35, adrenal cortical hyperfunction, a change in the electrophoretic pattern of the serum proteins, and a disturbance in the metabolism of vitamin B_{12}[8] will bring more strict rules for control of the diabetic patient and will necessitate further points to heed, in the control of the diabetic to save him from dreadful complications late in life Such a concept will critically affect our view of the new hypoglycemic agents, whether their effect is merely symptomatic, producing hypoglycemia, or truly physiological, correcting the over-all disturbance in the metabolism as insulin apparently does Finally, this view assigns responsibility to the treating physician, since his job will be not only to avoid the immediate fatal dangers of diabetes but also to guard against the later development of these complications

Summary

Three hundred and ninety-one diabetic patients were studied to demonstrate the factors responsible for the development of diabetic nephropathy A long period of uncontrolled, or inadequately controlled, diabetes was the prime factor responsible for the development of the lesions The sex, age, and severity of the diabetic state did not materially affect the development of these complications

Professor Ghaliongui and Dr Ghareeb kindly permitted the study of records of patients in the diabetic clinic

15, Buccleuch Place, Edinburgh 8, Scotland

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HYDRALAZINE POISONING

REVIEW OF THE LITERATURE AND AUTOPSY STUDY OF PERSON WITH MASSIVE INTESTINAL BLEEDING

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and
Carlos Ramirez, M D, Philadelphia

A 72 year old woman was hospitalized because of the sudden onset of hemorrhage during defecation On admission the patient was in shock, scattered petechiae and small purpuric lesions were seen on the skin of the lower half of the body, and the gastrointestinal bleeding continued She died on her fifth day in the hospital despite transfusions At autopsy pathological changes of the nature of fibrinoid necrosis were found throughout the body, including an appearance called wirelooping in the renal glomeruli This appearance is ascribed to a thickening of the basement membrane of the glomerular capillaries, which appear patent in the sections because of the rigidity of their walls All types of blood vessels were involved in a proliferative and necrotizing process The changes were attributed to poisoning with hydralazine, which the patient had been taking for hypertension in doses of 100 mg daily for two years

Since the first report [1] in 1952 of a grippe-like syndrome there have been over 80 recorded cases (2 14% of patients on long-term hydralazine [Apresoline] hydrochloride treatment for hypertension) of hydralazine poisoning in the English literature In the light of a postmortem examination revealing the presence of disseminated fibrinoid degeneration with necrotizing and proliferative vascular lesions in a recent case, a review of the literature is offered

This poisoning is the clinicopathological grouping of the multisystem symptoms and signs which relate to the long-term use of hydralazine It has been variously termed lupus erythematosus-like syndrome,[2] rheumatic syndrome,[3] hydralazine lupus erythematosus, hydralazine reaction, rheumatoid syndrome, and the rheumatogenic action of hydralazine Reviews of the pharmacology [4] and acute toxicity [5] (tachycardia, nasal flushes, burning of the face, and tingling of extremities) of hydralazine have been made The presence or absence of acute toxicity bears no relationship to the underlying pathology, natural course, or severity of hydralazine poisoning

The clinical onset occurs usually after 2 to 23 months [6] of therapy, which includes 200 to 800 mg of hydralazine daily Symptoms include chills, malaise, loss of weight, myalgia, muscle stiffness, arthralgia which is sometimes migratory, hematuria, pleuritic pain, abdominal pain,[3] fatigability, acute psychosis, diarrhea, gastrointestinal bleeding, sense of depression, glossodynia, and nocturnal itching of the knees and ankles

Among the physical findings, fever has been reported to reach a temperature of 105 F (40 C) Arthropathy may be generalized with hot, swollen, tender, and red joints which resemble rheumatoid arthritis particularly in the fusiform swelling of the proximal interphalangeal joints and may manifest joint effusion Among the skin eruptions, a butterfly rash has been seen Erythema of the hands [3] and severe erythematous reaction to ultraviolet light have been noted, petechiae and ecchymosis are occasionally found Also, tender muscles, pericardial friction rub,[6] tender lymphadenopathy,[2] hepatosplenomegaly,[7] subcutaneous nodules, and polyneuritis occur These symptoms and signs have occurred singly in varying combinations

In considering the laboratory findings, positive L E cell tests (peripheral and bone marrow methods) have been repeatedly reported,[3] but they may give negative results in patients with milder manifestations, one patient has been found to have a positive L E cell phenomenon without any sign or symptom of hydralazine poisoning [3] Biologically false-positive results of serologic tests for syphilis occur, reverting to normal within a month after treatment is discontinued A hyperglobulinemia of greater than 3 Gm involves an increase in both alpha-2-globulin and gamma globulin Comens [8] noted a decrease in cholesterol level in 88% of the patients Abnormal cephalincholesterol flocculation and thymol turbidity tests have been reported [6] as well as increased levels of serum polysaccharide and increased sedimentation rates Pancytopenia, leucopenia, and plasma cells in the peripheral blood have been noted A microcytic or normocytic anemia of 4 million cells or less have been found in as many

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Chief Medical Resident (Dr Bendersky) and Resident in Pathology (Dr Ramirez) Hahnemann Medical College and Hospital as 9 of 14 patients Dustan and others[9] described an interstitial pneumonitis with diffuse fine mottling resembling rheumatic pneumonia, two patients had transient pulmonary consolidation Three cases of polyserositis occurred The proteinuria and cylindruria attributable to nephrosclerosis subsided during the illness[7] The biopsy revealed the presence of acute collagenous necrosis of skin and subcutaneous nodule interpreted as a rheumatoid nodule[2] Interstitial polymyositis, muscle lymphorrhagia,[9b] and unexplained hemorrhages[7b] in the lungs, kidney, and intestinal mucosa have been seen The spleen has demonstrated periarteriolar increase of collagen in a laminated form[7b] Nasonova and Adyrkhaev[10] have demonstrated the presence of vasculitis during the use of hydralazine

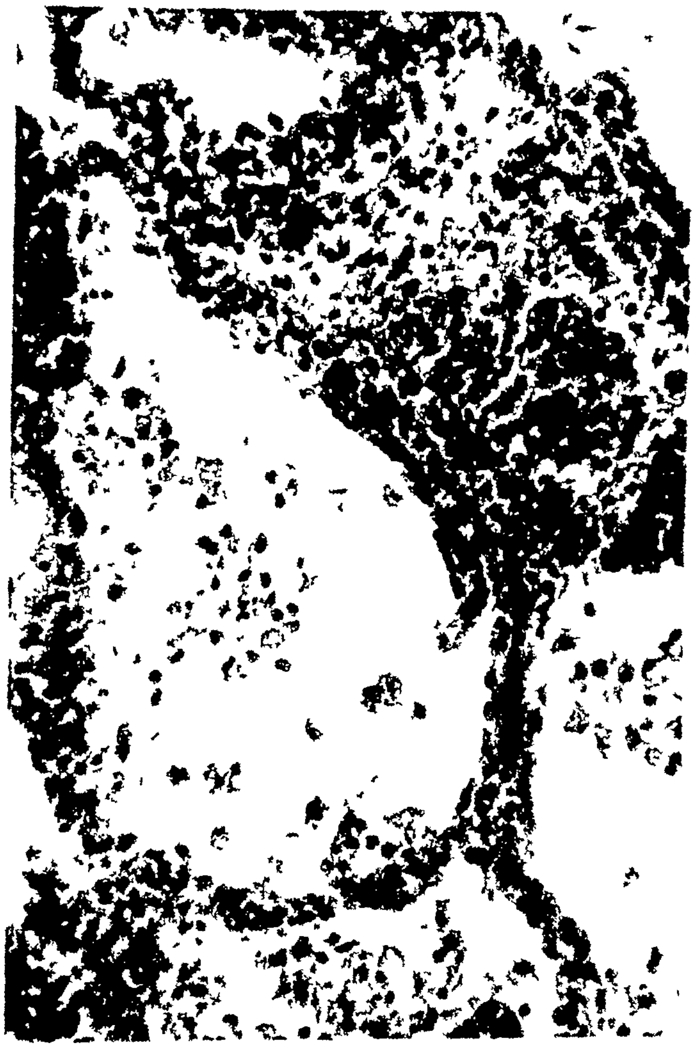

Fig 1 —Section of lung showing thickening of the alveolar walls by hyalinization and mononuclear infiltration Alveoli are filled with macrophages which form aggregates in some fields

The clinical course of hydralazine disease has been quite variable On discontinuance of the hydralazine therapy, symptoms have usually disappeared within a week, ranging from 24 hours to 4 weeks, in one patient they lasted 5 months Persistence of the signs and symptoms after withdrawal has been seen by others In one patient, the onset occurred five days after hydralazine was discontinued Temperature was recorded as subsiding while hydralazine therapy was continued[3] Abnormal findings returning normal last after discontinuing hydralazine have been the L E cell test and erythrocyte sedimentation rate, the L E cell finding has persisted as long as four months While hydralazine therapy is maintained, the initial malaise and polyarthralgia may be followed by a syndrome of hyperpyrexia, prostration, chest and abdominal pain, and physical-laboratory signs of disseminated lupus[3] The response of the febrile rheumatic state to adrenocorticotropic hormone, adrenal steroids and aspirin, or both, has been noted[9b] Consistent antihypertensiveness effectiveness of hydralazine therapy coinciding with the appearance of hydralazine poisoning is present in all but a few patients On resuming the therapeutic use of hydralazine after its previous withdrawal, single doses of hydralazine cause recurrences of similar manifestations, one patient has been described to have had a prompt recrudescence after three doses of 50 mg Some patients have no recurrences on resuming hydralazine therapy after a symptom-free interval, particularly at lower dosages

Report of a Case

A 72-year-old woman was admitted to Hahnemann Medical College and Hospital on March 30, 1958, because of the sudden onset of hemorrhage during her bowel movement She had been treated by her local physician for two years with hydralazine, 100 mg daily, for hypertension She had had no hemorrhoids, constipation, history of peptic ulcer, or hemorrhagic condition previously, there were no known allergies, hypertensive crises, congestive failure, hematuria, abdominal or chest pains, diarrhea, fever, arthralgia, or myalgia

On physical examination the patient was in shock, blood pressure was 60/40 mm Hg, temperature was 100 F (37 C) rectally, pulse was 140 per minute, and respirations were 18 per minute Retinal arterial tortuosity and minimal arteriovenous nicking were observed No distended neck veins were evident The heart and lungs were considered unremarkable Neither liver nor spleen was palpable No lymphadenopathy was discernible Scattered, nonconfluent petechiae and small purpuric lesions were found on the skin of the lower extremities and the inferior third of the anterior abdominal area, being more numerous in skin folds On proctosigmoidoscopic examination, actively continuing bleeding in the form of an accumulating pool of blood was seen and prevented a wholly satisfactory evaluation, although the source of bleeding was unknown, no mucosal purpuric lesion and no ulceration were found

Laboratory examinations revealed the following data an initial hemoglobin level of 6 4 Gm %, hematocrit value to 26 vol %, white blood cell count of 9,850 per cubic millimeter, a normal differential count, coagulation time (Lee White) of two minutes, and prothrombin time (one stage) of 100% A Rumpel-Leede test gave negative findings, platelet counts were of 250,000 and 180,000 per cubic millimeter, blood urea nitrogen level was 17 mg%, bleeding time (Duke) was three minutes, Kolmer test gave weakly reactive results (three units), Venereal Disease Research Laboratory test for syphilis gave negative results, clot retraction time was normal, total bilirubin level (after transfusions) was 2 6 mg, and a urinalysis gave negative findings An electrocardiogram on March 31, 1958, showed normal findings, except for frequent premature ventricular systoles A series of tests on the upper gastrointestinal tract gave normal results except for the incidental finding of opaque gall bladder calculi On March 31, the roentgenogram of the chest demonstrated cardiac enlargement and passive congestion An L E cell preparation was not performed

Although hydralazine poisoning was not suspected initially, this drug was discontinued on admission The patient received 4,000 cc of blood while active bleeding continued No hematemesis occurred No adrenocorticotropic hormone or adrenal steroids had been administered to this patient Twenty hours after the last unit of blood had been administered, acute pulmonary edema developed (April 1), which improved only transiently on digitalization and the use of morphine sulfate, oxygen, and aminophylline The patient died on April 3, 1958

Autopsy Findings

The body was that of a well-developed, well-nourished woman appearing about the stated age of 72 years There were scattered petechiae on the skin of both legs and lower abdominal wall, they were more apparent in the skin folds The peritoneum showed some bands of fibrous adhesions to the gall bladder and spleen The pleura of both lungs also showed multiple bands of adhesions, especially at both bases The heart weighed 380 Gm, the coronary arteries showed mutiple eccentric plaques of atherosclerosis, some of which were calcified The lungs were increased in weight, on section they showed a red congested surface The liver weighed 2,100 Gm, and its edge lay at two finger breadths below the right costal margin, on section diffuse nodular cirrhotic process was seen to involve the liver extensively The gallbladder contained multiple multifaceted dark green stones, the common and cystic ducts were patent The spleen weighed 790 Gm The mucosa of the last portion of the jejunum and that of the ileum was congested and revealed scattered shallow irregular ulcerations, varying in size from 2 to 8 or 9 mm The base of the larger ulcers was firm and covered by reddish granular tissue Section through the base of the ulcers revealed a reddish, slightly thickened intestinal wall The contents of the colon at these levels were slightly bloody, the mucosa of the colon was intact

The arteries of the mesentery revealed multiple eccentric plaques of atherosclerosis The esophagus, stomach, and duodenum were not remarkable The adrenals on sectioning displayed small areas of hemorrhage in the medulla The kidneys were slightly larger than normal, the capsule was thin, stripped with ease, and left a finely granular surface with some irregular, shallow scars and a few petechiae The aorta revealed multiple plaques of atherosclerosis, some of which were ulcerated and covered by thin mural thrombi The splenic, renal, and cerebral arteries were also sclerotic

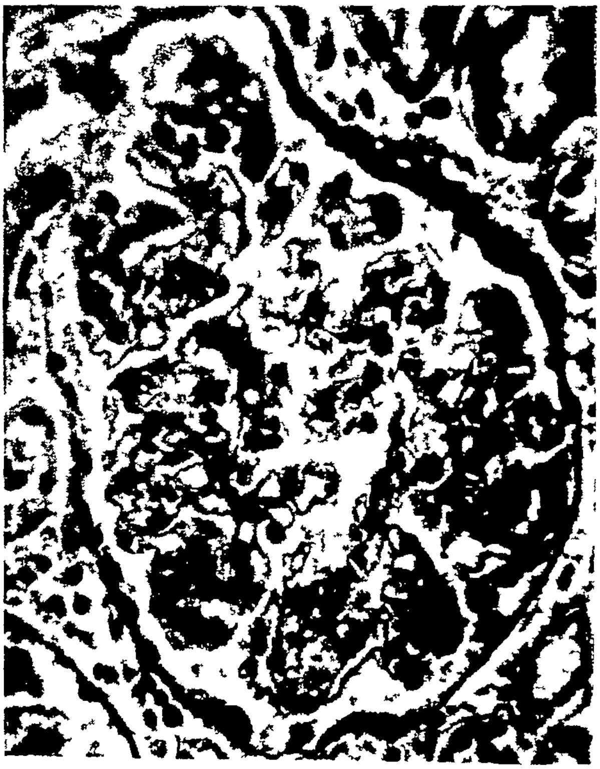

Fig 2 —View of kidney glomerulus showing thickening of capillary basement membranes and patency of capillary lumina due to rigidity of walls This presents the 'wire-loop appearance characteristic of lupus erythematosus cells Bowman's capsule also reveals hyaline thickening

Microscopically, the heart sections showed diffuse areas of myocardial fibrosis and proliferation of the mesenchymal cells in the interstitial spaces There were foci with moderate fibrinoid degeneration of collagen in the interstitial tissue of the myocardium, the arterioles of which showed focal areas of fibrinoid swelling and necrosis of the wall The coronary arteries showed plaques of intimal fibrosis and hyalinization, calcification was present and occurred at the junction of intima and media (fig 1) The subpleural layer of connective tissue was moderately distorted due to an increase in perilobular connective tissue There was infiltration of the hepatic connective tissue by numerous lymphocytes and plasma cells The sinuses of the splenic pulp were prominent and dilated There were swollen, hyalinized bands of collagen forming concentric laminations around the penicillary arteries In the kidneys, the glomeruli revealed focal acidophilic and homogeneous thickening of the basement membrane of the glomerular capillaries (fig 2), this change consisted of an eosinophilic fibrinoid "wire loop" of segments of capillaries which involved isolated glomeruli and isolated portions of the glomeruli of both kidneys

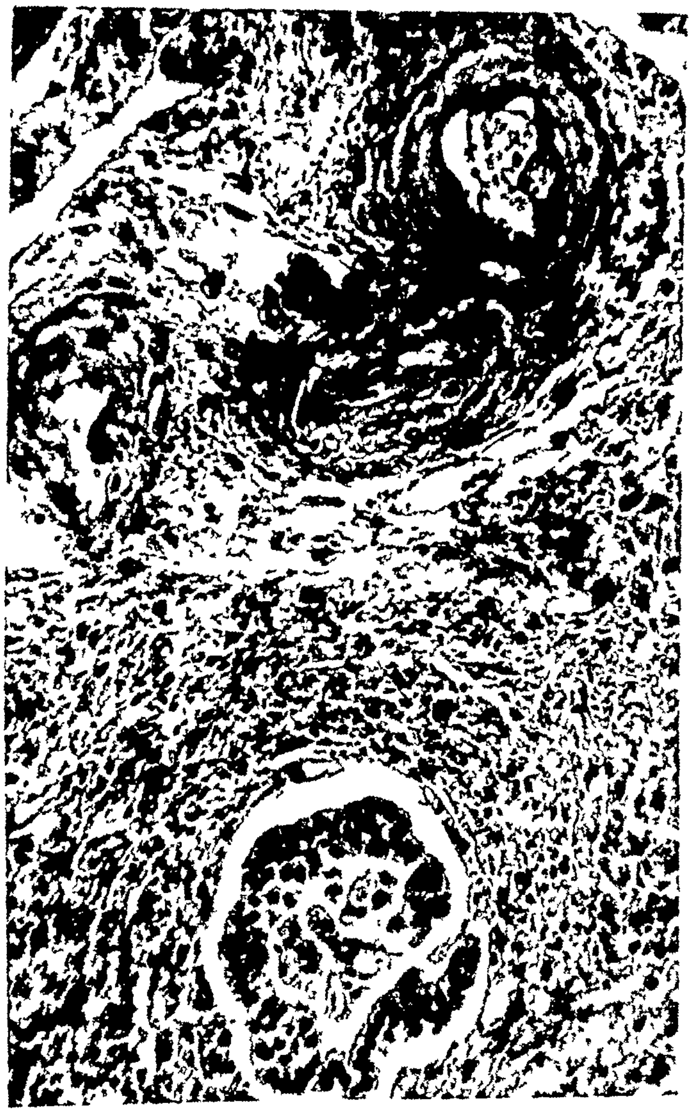

Fig 3 —Section showing several blood vessels in adrenal capsule Walls are thickened by hyalinization, and lumen is narrowed in two and occluded in one

The involved areas of the glomerular capillaries took the periodic acid–Schiff stain and appeared as a purplish-red broadening, and irregularity of the basement membrane, reticulum stain showed areas of fragmentation of the fibers, while the Luxol blue stain was unremarkable Characteristically, the vas afferens arterioles did not show any arteriosclerotic change The medium sized renal arteries present arteriosclerotic changes and thickening of the medial and subendothelial fibrous proliferation The convoluted tubules showed cloudy swelling The adrenal arteries and some of the arterioles in the periadrenal fat showed thickening and fibrinoid changes of their walls and also focal areas with chronic inflammatory cells (fig 3) The jejunum and ileum showed superficial ulcerations of the mucosa, areas of hemorrhage, and areas covered by granulation tissue Both mucosa and submucosa were infiltrated with acute and chronic inflammatory cells which, in some portions, extended to the muscularis Some of the medium sized arteries of the submucosa showed thickening and fibrinoid degeneration of the medial and intima as well as mononuclear cell infiltration (fig 4 and 5) The original fibrous, muscular and elastic elements of the intima of the aorta were replaced by a mixture of hyaline material, cholesterol needles, calcium deposits and blood The media subjacent to the plaques was also involved, and only one-half of the normal depth of the coat was left

Comment

Following a review of the literature dating since the introduction of hydralazine into the treatment of hypertension, we found that this was the first autopsy study that demonstrated the extensive fibrinoid necrosis including the renal glomerular "wire-looping" which are attributable to hydralazine poisoning In an autopsy study Dammin and others[7b] reported periarteriolar increase of collagen, glomerulonephritis, and interstitial polymyositis, but no necrosis of arterioles was found Although no L E cell test was performed on our patient, the finding of necrotizing and proliferating vascular lesions including the wire-loop glomeruli were highly suggestive of disseminated lupus erythematosus The inciting role of hydralazine seemed acceptable as established by Perry and Schroeder[8] and others[11] Scleroderma which may cause "wire loop" renal changes usually presents findings which were not present in our case Although the onset at the age of 72 might further tend to support the view in this case that an inciting factor precipitated the pathological manifestations, it has been reported that the initial onset of spontaneously developed disseminated lupus can occur in this age group[12] It is particularly noteworthy that despite the extensive fibrinoid necrosis and vascular involvement in this patient, the presenting clinical manifestations were minimal in number petechiae, intestinal bleeding, and congestive failure (the latter being precipitated probably by combination of myocardial fibrosis, fibrinoid and collagen degeneration, ischemia, and perhaps overzealous blood replacement) Also interesting was the absence of prodromal fever, myalgia, or arthritis The arteriolar changes of arteriosclerosis in our patient were considered discernible histopathologically from the coexisting collagenous abnormalities and fibrinoid degeneration Clinically, too, the absence of any feature of malignant hypertension tended to eliminate the possibility of the necrotizing changes being caused by the hypertension These were significant points in view of the difficulties expressed by some in distinguishing fibrinoid lesions of acute malignant hypertension from those of collagen disease

From this case the observation has been made that doses of hydralazine as low as 100 mg for prolonged periods of time may not be innocuous Reynolds and Caldwell[13] reported a patient who took 100 mg daily for four weeks, and McNicol and Hutchison[14] cited a case in which a patient was given a dosage of 50 mg daily for one week and then 100 mg for two weeks, the drugs were considered pathogenic Further elucidation in this regard will have to be accomplished before implications can be drawn concerning the continued usage of the drug in the lower dosage in persons already demonstrating hydralazine poisoning Dustan and others[9b] continued their patients on hydralazine therapy at 150 to 300 mg daily and aspirin for recurrent mild arthralgia

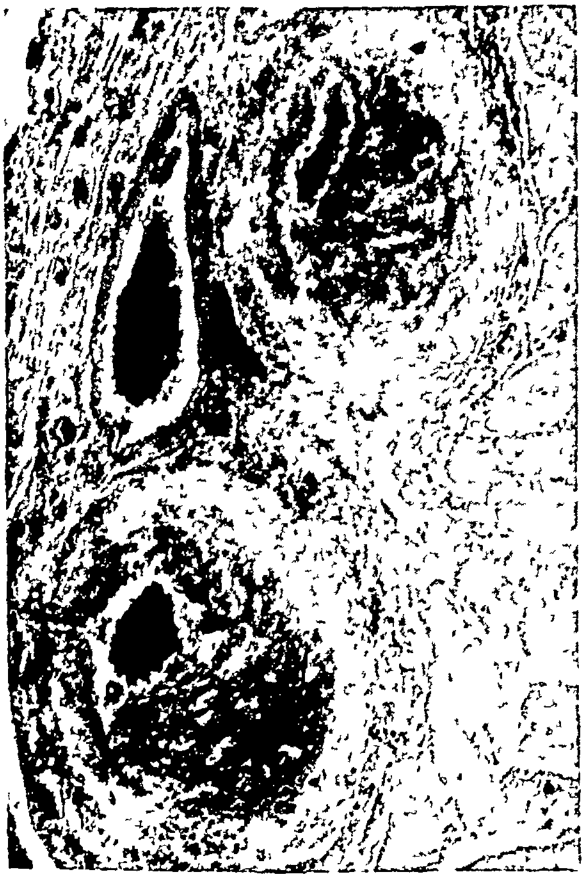

Fig 4—View of small intestine wall showing two arteries and eccentric thickening of the wall which narrows the lumen Thickening is due to large amount of fibrinoid degeneration which involves intima and media Note destruction of internal elastic membrane There is minimal cellular reaction, it consists of mononuclear infiltration about and in vessel wall Many veins are dilated and congested with blood The overlying mucosa is not intact

Our patient also represented the first death due to intestinal hemorrhage resulting from mucosal ulcers induced by vascular fibrinoid changes attributable to hydralazine poisoning Spontaneous massive intestinal bleeding can occur without the use of adrenal steroids and without prodromal warning signs Several other cases[7b] of gastrointestinal bleeding from hydralazine poisoning have been reported but none demonstrably due to fibrinoid or collagen abnormalities Of cases of disseminated lupus erythematosus not associated with the use of hydralazine, gastrointestinal manifestations have been prominent as classically described by Osler In Dubois' cases[15] of lupus erythematosus, occasional bloody diarrhea was noted Of the 138 cases of Harvey and others,[12] three patients had acute arteritis with thromboses of small vessels, which resulted in ulceration and hemorrhage of the small intestine In other conditions known as collagen disease, gastrointestinal bleeding from necrotizing arteritis is well documented About 5% of cases of thrombotic thrombocytopenic purpura cause gastrointestinal bleeding associated with endothelial proliferation and thrombosis Of 30 patients dying with periarteritis nodosa on whom postmortem examinations were performed at the Mayo Clinic, 21 had bleeding, including hemorrhagic lesions in the duodenum and upper jejunum and ulcerative lesions of the small and large intestine[16] In Arkin's series[17] of patients with periarteritis, 50% had gastrointestinal lesions and 30% had mesenteric arterial involvement Gross hemorrhage into the gastrointestinal tract of periarteritis patients has occurred in association with ulcers caused by the blood vessel pathology in the jejunum or colon In a review[18] on dermatomyositis, 10 cases are described with intestinal tract involvement, one patient had bleeding associated with sharply punched out ulcers throughout the entire jejunum and pronounced fibrous intimal thickening of large and mediumsized arteries Similar findings are present in acute vascular purpura (Schoenlein-Henoch syndrome)[16] and systemic progressive sclerosis (visceral scleroderma)

As judged by clinicopathological resemblances, interrelationships between the various collagen diseases have been previously noted Some of the cases of hydralazine poisoning are not typical of disseminated lupus or rheumatoid arthritis and particularly may resemble periarteritis nodosa or necrotizing angiitis[3] That difficulty should arise in assigning a specific collagen diagnosis to hydralazine poisoning is not surprising in view of both the generalized character and multiplicity of clinical and microscopic findings characteristic of this group of diseases as well as the recognized histopathological interrelationships and coexistences of the collagen diseases Particularly the *angiitis and* perivascular changes are features in common with periarteritis nodosa, lupus erythematosus, rheumatoid arthritis, rheumatic fever, vascular purpura, dermatomyositis, and scleroderma

Summary and Conclusions

A case has been presented of a 72-year-old woman who had hydralazine poisoning, death was associated with the massive intestinal bleeding and mucosal ulcers resulting from necrotizing vasculitis and fibrinoid degeneration Autopsy study revealed the pathological basis for hydralazine poisoning in this patient to be proliferative and necrotizing involvement of the arterioles and arteries of the myocardium, kidney, spleen, jejunum, and ileum in the absence of malignant hypertension The "wire-loop" glomerular thickening along with other features suggest that this case resembled more disseminated lupus in the spectrum of diseases of the *collagen type The low dosage of* hydralazine, the paucity of clinical features in the absence of prodromal fever or arthropathy, and a short clinical course were discordant with the prominence of the postmortem findings The implications of the asymptomatic development of a fatal, drug-precipitated disorder are drawn

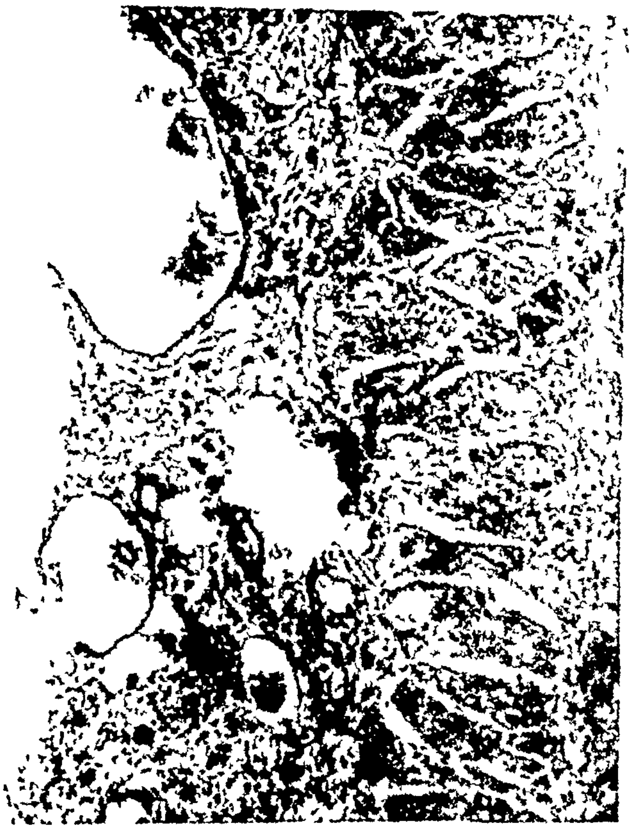

Fig 5—View of small intestine directly adjacent to the vessels seen in fig 4 showing loss of mucosa and thickening of submucosa due to dilatation of veins, edema, and cellular infiltration Some vessels are obviously ruptured and account for hemorrhage

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SURVIVAL OF PATIENTS WITH CANCER OF THE THYROID GLAND

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and
Sidney J Cutler, M A, Bethesda, Md

During the period 1935 to 1951, there were 283 newly diagnosed cases of thyroid cancer among residents of the state of Connecticut The median survival after diagnosis for the 251 persons with histological confirmation of cancer was three and one half years At the end of the 12th month, two thirds of the patients were still alive, whereas two thirds of the members of a control group had not yet died by the end of the 12th year Thyroid cancer progresses five times more rapidly in men than in women Women with papillary cancer have a considerably better prognosis (median survival nine and one half years) than women with the non papillary variety (median survival two years) The survival of men was poor regardless of the histological variety of the neoplasm For both sexes combined the median survival in localized thyroid cancer was four and one half years for the nonpapillary types and eight years for the papillary variety

A previous communication [1] stressed the fact that cancer of the thyroid was encountered in the urban population of the United States more frequently than was hitherto suspected According to the study on morbidity from cancer conducted by the National Cancer Institute on about one-tenth of the population of the United States,[2] cancer of the thyroid accounted for 336 of the 46,390 neoplasms newly diagnosed in 1947 This means that if the findings derived from the surveyed areas are representative of the whole United States about 4000 new cases of thyroid cancer are likely to develop annually throughout the country Thus, the number of persons attacked by thyroid cancer is far from being negligible, and an estimate of how long they survive their disease appears desirable

It is essential that a study of this sort be based on the outcome of all the cases diagnosed among the residents of a given community regardless of the type of treatment they received and, for that matter, regardless of whether any was offered, accepted, or even available The interplay of these considerations is perhaps almost as significant for longevity as the development of the original cancer In fact, the death of a person who, having refused treatment, succumbs to a curable cancer represents a failure in any program of cancer control, and the fact that his demise was mediated or accelerated by his own lack of foresight does not make such failure less disappointing Therefore, cases of this sort should not be excluded when one attempts to evaluate the impact of cancer on the longevity of a community

The experience of any one clinic or hospital usually affords information only on the material seen in that particular place As there is no certainty that this material represents the totality of the cases occurring in the population served by that one institution, extrapolation from data of this sort to an entire community might prove hazardous Moreover, the lack of uniformity in the therapeutic approaches practiced in different hospitals adds to the uncertainty of conclusions based on selected material Difficulties of this sort can be overcome to a great extent if practically every single case of cancer diagnosed in a community is included in the study Thanks to the foresight of Dr M H Griswold, Chief of the Division of Cancer and Other Chronic Diseases, Connecticut State Department of Health, to whom we are indebted for the material on which this report is based, this exceptional situation exists in Connecticut

Since 1935 all cancer cases diagnosed in 30 of the 37 general hospitals licensed in the state have been collected in a central register These hospitals account for 94% of approved general hospital beds

Distribution of 283 Newly Diagnosed Cases of Thyroid Cancer by Sex, Microscopic Confirmation and Histological Type in Connecticut, 1935 to 1951*

	Both Sexes No	Men No	Women No
Total number of cases	283	71	212
Cases not microscopically confirmed	32	9	23
Cases microscopically confirmed	251	62	189
Papillary	79	17	62
Nonpapillary	172	45	127†

* Excludes death certificates only
† Includes seven cases of lymphoma and reticulum cell sarcoma

This information is supplemented by the records on cancer diagnosed among Connecticut residents sent to the Cancer Register from three hospitals and various agencies outside the state and by data obtained from mortality records

Material and Method

The 283 cases of thyroid cancer, newly diagnosed and reported by hospitals among Connecticut resi-

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From the Department of Preventive Medicine University of California School of Medicine (Dr Mustacchi) and the Biometry Branch National Cancer Institute National Institutes of Health (Mr Cutler) dents during the period 1935 to 1951, form the basis of this study. Of these, 9 out of 10 were histologically confirmed. The nonpapillary diagnoses outnumbered the papillary ones by a ratio of about 2:1 (see table). An actuarial or modified life table method[3] was used to calculate survival rates and cumulative percentage of survivors for each six-month follow-up period. Patients not included in follow-up studies or withdrawn alive during the period of study were assumed to have left the series at the midpoint of the appropriate six-month interval. Inasmuch as this study aimed at evaluating the longevity of the entire group, patients who had died of thyroid cancer or from some other condition were not treated separately. Expected survivals reported in this paper were calculated for each person on the basis of the data for the white population between 1939 and 1941 in the United States.[4]

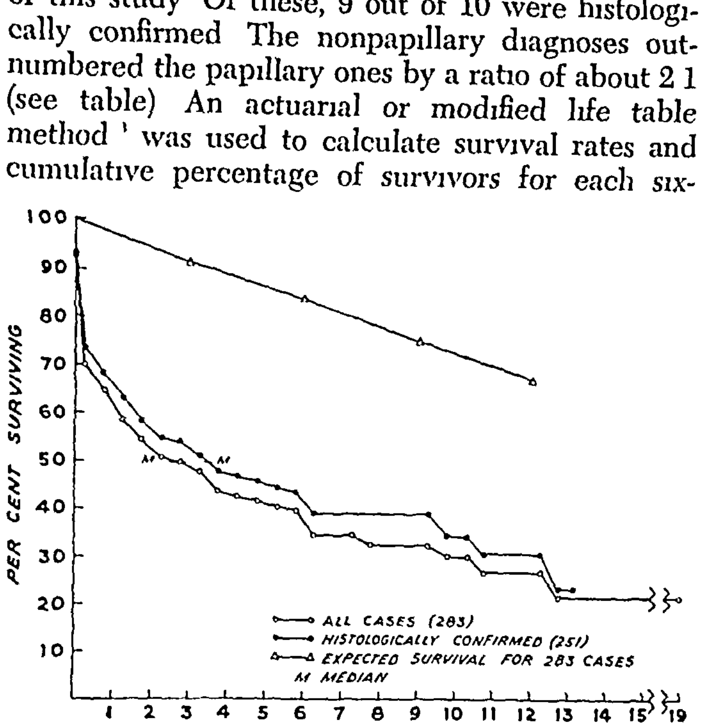

Fig 1.—Observed and expected survival of patients of both sexes with thyroid cancer in Connecticut, 1935 to 1951.

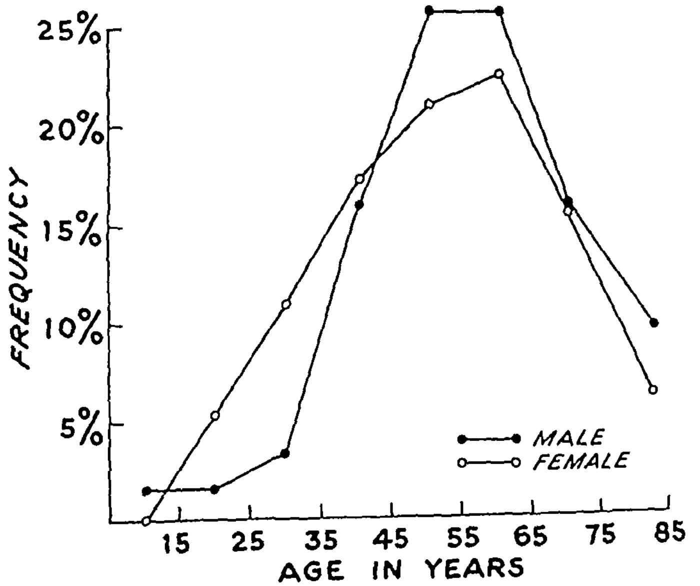

Fig 2.—Relative frequency of thyroid cancer, histologically confirmed, by age and sex in Connecticut, 1935 to 1951.

Results

Survival of the Group as a Whole.—The mortality experienced by the 251 patients with microscopically confirmed thyroid cancer was considerably greater than would have been expected for a group of the same age and sex distribution drawn at random from the general population (fig 1). In the control population, 68% of the persons could be expected to be alive at the end of the 12th year of observation, while the *same proportion* of the persons with cancer were still alive by the end of the 12th month. The median period of survival for this cancer group was about three and one half years after diagnosis.

It is of interest to consider the effect of including the 32 cases, the diagnosis of which was based on clinical but not on histological evidence. It can be seen that the mortality rate experienced by the total group of 283 is more severe than for the group of the 251 histologically confirmed cases. This difference shows up in the very first part of the follow-up period. It seems likely that the physicians reporting the 32 cases not ascertained histologically believed that their patient's clinical status was already so precarious that it did not warrant even the minimal risk of a biopsy. The early mortality experienced by these 32 patients seems to support this conjecture. At the same time it fortifies the belief that when microscopic confirmation is present in a majority of cases and histological variants are not parameters of an epidemiologic study on cancer the exclusion from the computations of those cases diagnosed only on clinical grounds may materially understate the magnitude of the problem.

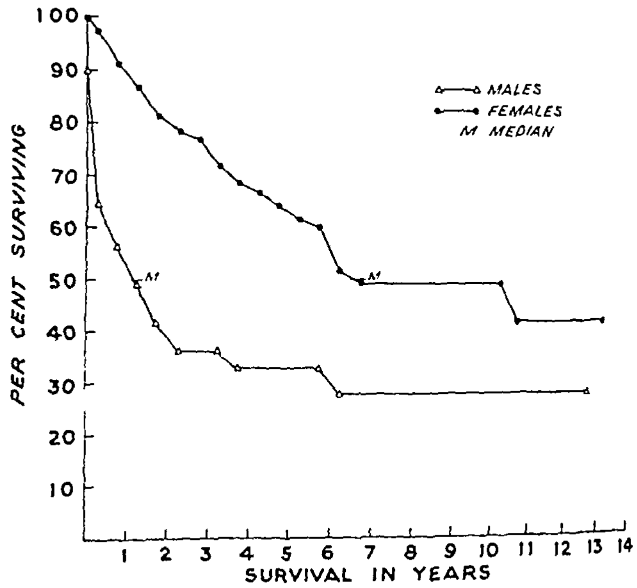

Fig 3.—Survival of patients with thyroid cancer, histologically confirmed, by sex in Connecticut, 1935 to 1951.

Survival of Patients with Histologically Confirmed Cases by Sex.—In agreement with data on thyroid cancer in other parts of the United States,[5] the Connecticut data indicate that this condition attacks women more often than men. The ratio of men to women is 1:3 among the patients with histologically confirmed cases. The age distribution curves (fig 2) have similar configurations for each sex, and the proportion of papillary neoplasm is fairly similar in both sexes (slightly less than one-third in women, slightly over one-fourth in men).

Although these aspects are comparable, cancer of the thyroid appears to be a much more lethal condition in men In fact, the median survival period for women was five times as long as the median survival time for men (fig 3) If further studies in other communities should indicate that this peculiarity is present elsewhere, then the observed lower rate of thyroid cancer incidence in men coupled with a much higher case fatality rate would indicate that the factors that favor or excite the development of a new cancer are not necessarily identical with those that stimulate the growth of one already existing

Survival by Sex and Histological Pattern—The finding that cancer of the thyroid runs a more aggressive course in men than in women stimulated a consideration of whether a different prognosis could be attached to the papillary and nonpapillary varieties Clinical observations testify to the exceptional longevity of women with a papillary carcinoma of the thyroid The Connecticut data support this (fig 4), in fact, the median survival for women with this variety of neoplasm amounted to nine and one half years, while in those with a nonpapillary variety it was barely over two years The poorer prognosis of men with thyroid cancer is evident also from an analysis of the survival of those attacked by either of the two major histological variants In men, the median survival for those with nonpapillary cancers was a little less than one year and for those with the papillary variety two years or slightly more It would seem from these data that the differential aggressiveness of the two major histological variants of thyroid cancer is not so manifest in men as it is in women

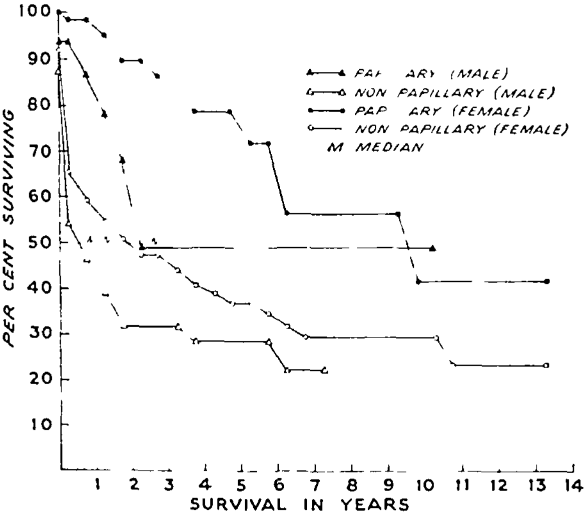

Fig 4—Survival of patients with thyroid cancer by sex and major histological patterns in Connecticut, 1935 to 1951

Survival in Localized Papillary and Nonpapillary Cancer of the Thyroid—A better survival was experienced by the groups whose thyroid cancer was localized, regardless of the histological pattern This was verified for both sexes combined as well as for women only Too few men with localized papillary or nonpapillary cancer existed in the Connecticut series to warrant analysis of the two types separately For both sexes combined, the median survival period in localized thyroid cancer was four and one-half years for patients with the nonpapillary types and nine and one-half years for patients with the papillary variety (fig 5) Parallel values are obtained when one calculates the survival period for women only The survival of women with localized papillary cancer of the thyroid approximates rather closely the "normal" survival curve (fig 6)

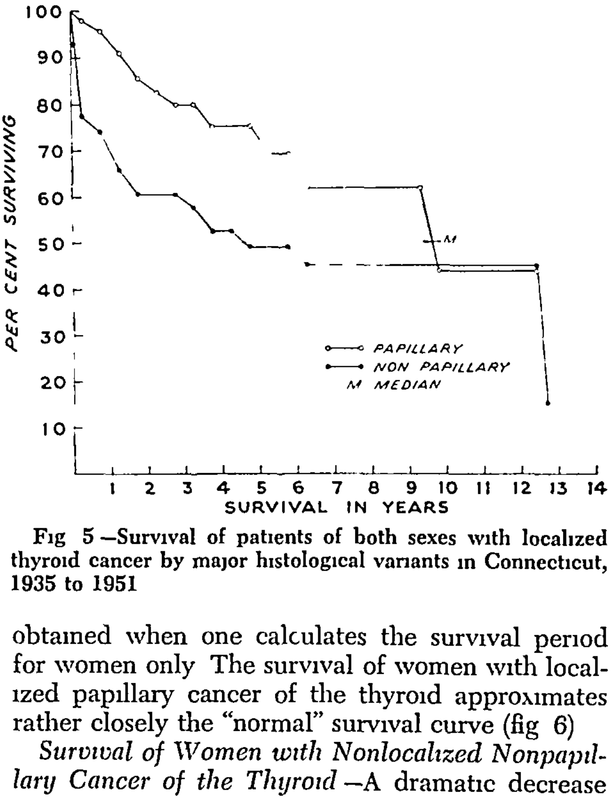

Fig 5—Survival of patients of both sexes with localized thyroid cancer by major histological variants in Connecticut, 1935 to 1951

Survival of Women with Nonlocalized Nonpapillary Cancer of the Thyroid—A dramatic decrease in life expectancy is associated with an extension of the malignant neoplasm beyond the thyroid gland It was mentioned that, for persons with the localized nonpapillary types, the median survival period was just under four and one-half years The median

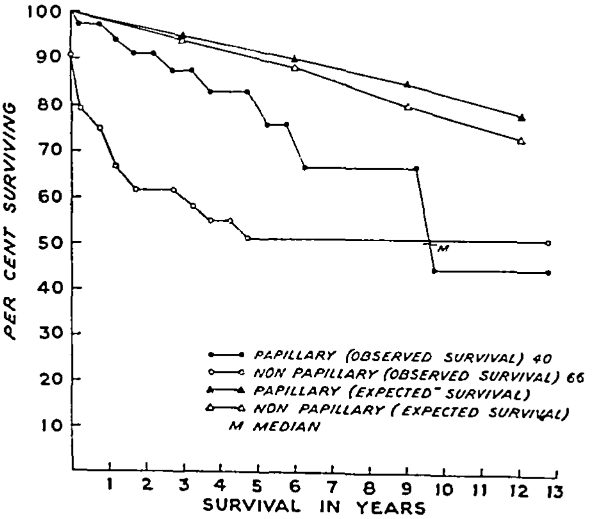

Fig 6—Observed and expected survival of women with localized thyroid cancer by major histological variants in Connecticut, 1935 to 1951

survival period was less than one-half of this time, or 21 months, when regional lymph nodes were involved, and it was reduced to less than three months when remote metastases were present (fig 7)

Question of Treatment as It Affects Survival—It was said in the introductory remarks that the main purpose of this presentation was to provide data on the present survival from cancer of the thyroid in an entire community regardless of the mode of therapy In addition, because of the variations likely to exist in the mode and extent of therapy chosen by the individual physicians of an entire state, it was felt that it might have proved hazardous to try to evaluate the advantages of any given mode of treatment for every given type or stage of the disease In only one instance it is felt that perhaps some fruitful conclusion could be reached The group of women with nonpapillary cancer of the thyroid was divided into two subgroups according to whether or not the surgical procedure the patients underwent included a resection of the regional metastatic nodes It was noticeable that a higher survival rate prevailed among the subgroup that underwent more extensive surgery This situation was not altered if one excluded from the computations the women that did not survive the first six months after surgery (fig 8) This last correction was made in the belief that in some of these patients extensive surgery, although advisable in the opinion of the physician, could have been contraindicated by the patient's critical condition However, as was stressed in the earlier part of this report, these observation should be interpreted with caution because of the known difficulties that attend the analysis of selected material

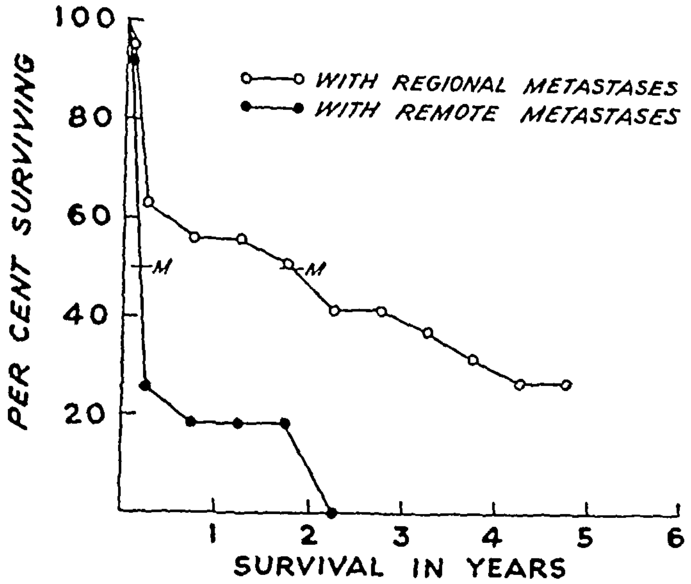

Fig 7—Survival of women with nonlocalized nonpapillary thyroid cancer by stage of disease in Connecticut, 1935 to 1951

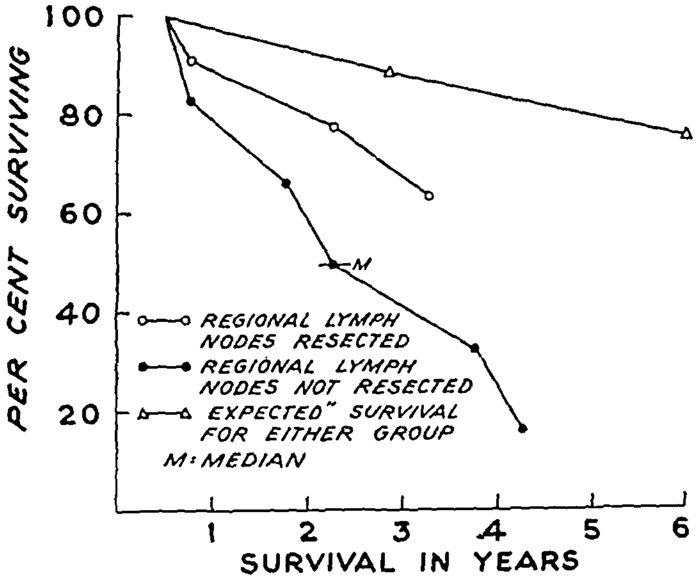

Fig 8—Survival of women with nonpapillary thyroid cancer with regional metastases by type of surgical procedure in Connecticut, 1935 to 1951 Study does not include patients who died within six months after diagnosis

Summary

During the period 1935 to 1951, 283 cases of thyroid cancer were reported to the Connecticut State Cancer Registry In this group, women outnumbered men in a ratio of 3 1 The analysis of the survival experience of these 283 patients reveals that thyroid cancer is more lethal in men than in women The median survival time for women is five times the median survival for men

In women a marked difference is noted in survival with respect to histological type The median survival time for papillary cancers was 9 5 years whereas it was barely over two years for the nonpapillary variety In men the survival time for both groups was shorter than in women and the difference between the two groups was considerably less, i e, there was a median survival of a little over two years in the group with papillary thyroid cancer and a median of under one year for those with nonpapillary thyroid cancer These findings may be interpreted as indicating that the factors responsible for the development of thyroid cancer in man differ from those that condition its subsequent growth

Parnassus and 3rd Avenues (22) (Dr Mustacchi)

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SUBACUTE THYROIDITIS

WITH SPECIAL EMPHASIS ON THE PROBLEM OF EARLY RECOGNITION

Robert J Vanderlinde, M D
and
John Milne, M D , Hanover, N H

Subacute thyroiditis often escapes recognition, although the diagnosis is easy if the possibility is kept in mind Of the 13 cases summarized here, only 6 were diagnosed by the first physician who saw the patient, and in 3 cases it was the fourth physician who made the diagnosis The most important diagnostic clue was palpation of the thyroid, which would often have sufficed to distinguish between thyroiditis and pharyngitis The disease is generally self-limited, and patients with mild cases need only aspirin Steroid therapy is purely symptomatic In most patients it brings about relief from pain, swelling, and fever within the first day or two One patient had relapses on three occasions when it was discontinued or the dose lowered prematurely

Subacute thyroiditis was described over 50 years ago and was most completely delineated in 1936 when de Quervain and Giordanengo [1] wrote about it for the second time so well that it is still referred to by de Quervain's name The principal features of the usual case include fever of mild to moderate severity, pain in the neck noted especially on swallowing and often referred to the ears, at time symptoms of hyperthyroidism, and most important, a swollen, tense, tender thyroid gland Most often the entire gland is involved, but at times only one lobe may be swollen and tender when the patient is first seen Later the process usually spreads to involve the other areas In addition, one typically observes tachycardia, sweating, and often an anxious or distraught patient when the disease has gone undiagnosed Some of these clinical findings may be present over a period of weeks or even many months in the untreated patient

One might justifiably conclude that with such a relatively characteristic combination of symptoms diagnosis is easy This may perhaps be true, but the fact that the diagnosis, even in a typical case, is often not readily made is a reason for our interest in this disease A review of our recent experience with this disease is presented with emphasis on the problems of early recognition

The incidence of the disease seems to vary both with the geographical zone and with the interest of the observers In general, the number of cases appears to be considerably higher in the west than on the eastern seaboard of the United States The recognition of several cases in the same neighborhood in New York City within a short span of time [2] suggests an infectious process or a disseminated causative agent For years there has been speculation that the disease is of viral origin This has been supported by the clinical features of the illness, by the failure to isolate bacteria from the thyroid tissue of the patients, and by the histological appearance of the thyroid gland Of most importance in this respect is a recent report from Israel [3] In a two-year period 15 cases of subacute thyroiditis were diagnosed Ten of 11 patients with subacute thyroiditis had positive results of complement-fixation tests against mumps virus that were shown to be almost certainly not anamnestic reactions In two patients a virus which could not be distinguished from mumps virus was isolated from thyroid tissue with the technique of specific inhibition of hemagglutination Thus, perhaps for the first time at least one causative agent has been identified Mumps virus may involve salivary, pancreatic, testicular, mammary, ovarian, and now the thyroid glandular tissue In none of the cases occurring in Israel was there simultaneous involvement of the salivary glands and the thyroid, however, abdominal pains were common, and tests in three of six cases showed elevation of blood diastase levels

This disease is said to appear about one-eighth as often as hyperthyroidism [4] and perhaps less often than Hashimoto's struma We have not found such a high incidence as this when compared to hyperthyroidism The incidence of subacute thyroiditis in the Hitchcock Clinic in recent years has varied from one to three cases per year that were diagnosed without operation Another one to three cases each year can be added to this figure if we include the patients operated on for diagnostic purposes when thyroiditis was either unsuspected (fig 1) or not sufficiently typical to be diagnosed on nonhistological grounds only Most often these patients were operated on because of suspected cancer It should be stated that some of our records that include the diagnosis of "chronic thyroiditis" made by histological examination include some cases that may well be late stages of subacute thyroiditis The delineation of the histological picture, while often described as being easy, may pose problems in specific instances

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From the Hitchcock Clinic and the Dartmouth Medical School

Portions of this paper were read before the New Hampshire Vermont Medical Society Annual Session October 1959 Manchester Vt

In order to relate the clinical features of the typical symptomatic case to the disturbed function of the gland, a review of the records of consecutive patients most recently seen in our clinic was undertaken As a result of this study three questions were raised, the answers to which are of general interest 1 What symptoms bring the patient with subacute thyroiditis to the physician? 2 How long have the symptoms gone unrecognized as being due to subacute thyroiditis? 3 How many physicians examined the patient(s) before the diagnosis of subacute thyroiditis was made?

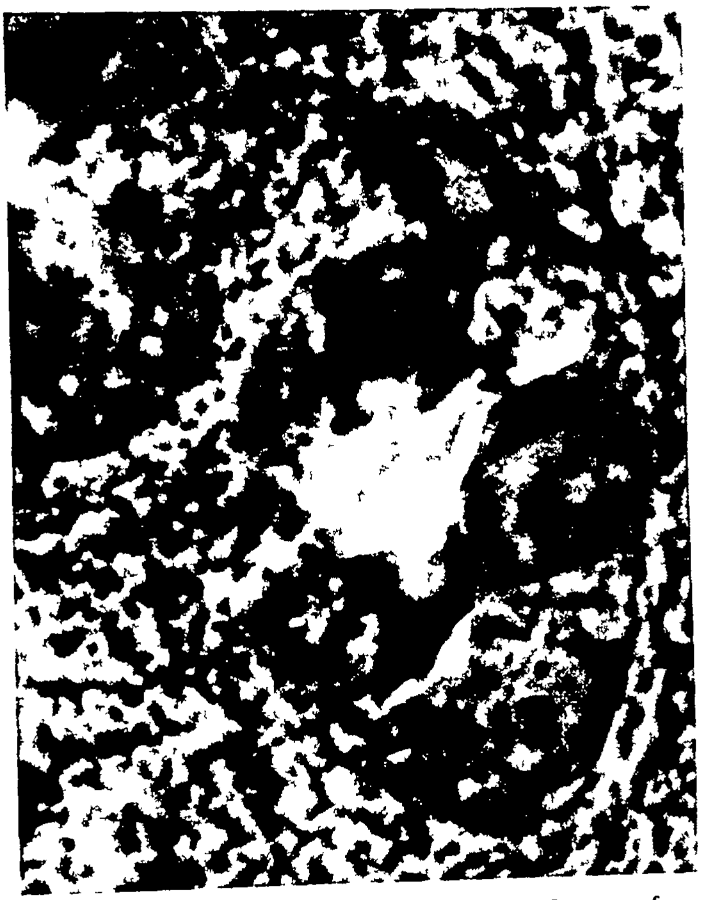

Fig 1 —Microscopic appearance of thyroid mass of patient presenting without typical thyroiditis symptoms Appearance is that of subacute thyroiditis with loss of follicular structures, cellular infiltration, production of fibrous tissue, and several giant cells

The opening remarks of the patient as recorded in the history almost always referred to "pain in the neck," or "sore throat" (see table) These symptoms existed from a day or two to several months before the patient sought medical attention The subsequent lag before a correct diagnosis was made (or suggested) was variable, as was the number of physicians who had examined the patient without suggesting the correct diagnosis Three points are of interest 1 In all but one instance in which the diagnosis was overlooked the records do not specifically indicate that the thyroid gland was palpated prior to the examination by the physician who made the correct diagnosis 2 In most instances in which the diagnosis was promptly made by the first physician who saw the patient, he had seen a patient with subacute thyroiditis within the preceding year 3 Most incorrect diagnoses were in the general category of conditions such as pharyngitis, sore throat, and others In essence, whenever disease of the thyroid was first considered, the correct diagnosis was usually made

In normal conditions the thyroid gland, under stimulus of the thyrotropic hormone, secretes sufficient hormone in the form of thyroxin to maintain a euthyroid state As shown in figure 2, the normal gland extracts and traps iodide from the blood and converts it through a series of reactions to some such iodine-containing material as thyroglobulin In this process other iodinated compounds may be produced and escape from the gland, but in general the compounds that normally leave the gland in quantity are thyroxin and perhaps tri-iodothyronine The former is the usual major constituent of the protein-bound iodine (PBI) and also largely determines the basal metabolic rate Thyroxin and tri-iodothyronine, in turn, are principals in the regulation of thyrotropic hormone output by the pituitary gland

The effects of subacute thyroiditis on thyroid function and the clinical tests of thyroid function have been observed by many different investigators[5] The results of disruption of normal structure and function are as follows 1 There is a decrease in hormone synthesis During the early weeks of the disease this may be measured clinically, albeit somewhat indirectly, by the uptake of radioactive iodine (I^{131}), which is characteristically low This low rate of trapping and utilization of I^{131} may be reflected late in the disease by temporary findings of hypothyroidism The depressed uptake of I^{131} is not affected by doses of thyrotropic hormone that are sufficient to stimulate normal thyroid glands, although large doses given over several days do cause an increase in uptake in some instances 2 There is a release of iodinated material into the circulation as storage function is impaired This may result in an elevated protein-bound iodine level In

Consecutive Cases of "Symptomatic" Subacute Thyroiditis Seen at Hitchcock Clinic (1954-58)

Case			Type and Duration of Symptom Before 1st Examination	Diagnosis	
No	Sex	Age Yr		Interval Between First Medical Examination and Date	Made by Physician No
1	M	49	Pain in neck, 1 mo	3½ wk	4th
2	M	35	Sore throat and fatigue 5 days	None	1st
3	F	54	Tender thyroid 2 3 wk	2 wk	2nd
4	F	49	Swelling and pain in neck and pain in ears 10 days	None	1st
5	F	53	Painful swelling in thyroid area and fever, 48 hr	None	1st
6	F	31	Chills fever, and sore throat 3 wk	3 wk	2nd
7	M	33	Pain in ear and sore throat 1 wk	None	1st
8	F	64	Pain in neck and weakness 10 wk	6 wk	4th
9	F	58	Soreness and pressure sensation in neck 3 mo	5 days	4th
10	F	36	Pain in neck with radiation to ears and fatigue 1 wk	1 day	1st
11	F	32	Tender lump in neck 2 wk	2 wk	3rd
12	F	51	Painful swelling in neck 1 wk	4 wk	3rd
13	F	32	Sore throat, 7 days	1 day	1st

some cases there may be associated hyperthyroid symptoms and an elevated basal metabolic rate At times the butanol-extractable iodine (BEI) level has been observed to be considerably lower than that of protein-bound iodine, and in such instances the calorigenic effect of the excess iodinated material is relatively low compared to that of tri-iodothyronine and thyroxin

Other tests are helpful but are not specific in diagnosis The erythrocyte sedimentation rate is often elevated, and there is frequently an increase in alpha-2 globulin and fibrinogen levels, but one needs the patient's medical history and physical examination to interpret these findings[6] As yet the immediate diagnosis is not facilitated by immunologic studies or auto-immune antibody testing Perhaps some procedures for mumps or other viral tests may prove of diagnostic value in the future

It is apparent from the variety of treatments advocated for patients with subacute thyroiditis that therapy is nonspecific In general, steroid and radiation therapy are the treatments of choice The mere passage of time and therapy with aspirin also are of value in this condition Antibiotic therapy and surgery have not proved effective in treatment of subacute thyroiditis Other therapeutic agents used to treat this condition are iodides, propylthiouracil and similar substances, and thyrotropic hormone We have treated few patients with radiation in recent years (2 of a total of 13) This is probably due to the rapid response of the symptoms to steroid therapy One should not discard x-ray therapy, particularly in situations in which steroids are contraindicated, but at present the cost factor, the speed of-response factor, and the incidence of hypothyroidism all have inclined us to use adrenal steroids first Whether x-ray therapy should be used for this relatively benign disorder may be questioned by some persons Most patients obtain a dramatic alleviation of pain and subsidence of the swelling and fever within the first day or two of steroid therapy The therapy must, however, be maintained for some days and even up to one month or more to suppress the disease until it no longer flares when steroids are withdrawn No specific length of time can be set beforehand as an optimum for therapy, because each patient constitutes an individual trial of therapy

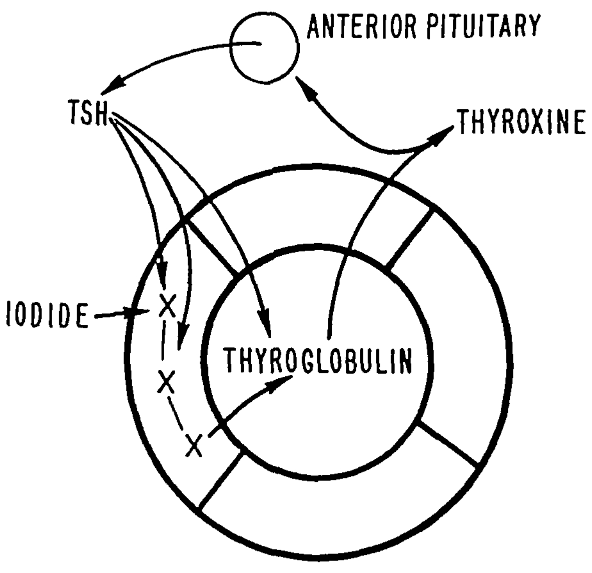

Fig 2 —Simplified version of relation between pituitary gland and iodine metabolism in thyroid Thyroid stimulating hormone (TSH) acts at several sites from extraction of iodide to release of thyroxin into circulation Output of TSH is decreased as that of thyroxin increases

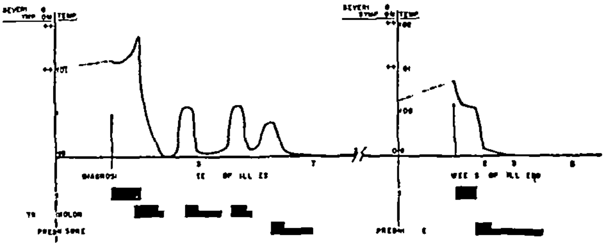

Fig 3 —Response of thyroiditis symptoms to steroid therapy *Left*, 35 year old male patient (case 2, table 1) *Right*, 36 year old female patient (case 10, table 1)

The contrasting clinical courses of two patients are shown in figure 3 They demonstrate that steroids apparently do not cure the disease but simply suppress the symptoms until the illness has run its course It can be seen that the patient in case 2 (fig 3, *left*) had relapses on three occasions when steroid therapy was discontinued or the dose lowered prematurely The patient in case 10 (fig 3, *right*) had a remarkably different response, although it is evident that treatment was started in both patients at about the same interval after the onset of symptoms

These patients get well We are unaware of any deaths caused by subacute thyroiditis Patients may be incapacitated for months and the disease may "grumble on' for even one year or longer Many instances of hypothyroidism have been described It is fairly clear, however, that when permanent hypothyroidism occurs, either the patient had part or most of the gland resected as in the 12 patients with hypothyroidism reported from the Mayo Clinic,[4] or the patient had a large dose of radiation therapy, often considerably in excess of the recommended maximum of 600 to 800 r Permanent hypothyroidism in the patient treated with steroids, or aspirin—and aspirin may be all that is required in some cases[7]—must be as rare as it is in untreated patients This is in contrast to the Canadian report of the high incidence of temporary hypothyroidism that follows severe subacute thyroiditis[5b] It is the rare patient in our group who developed this temporary hypothyroid state, although we could well have overlooked the condition when a patient was not seen at frequent intervals after the major thyroiditis symptoms had subsided

Summary

An analysis of the recent experience with subacute thyroiditis at the Hitchcock Clinic shows that there is good reason to believe that the disease is more common than our statistics would indicate The diagnosis may be overlooked and the patient treated for pharyngitis, or some similar condition, while the thyroiditis runs its clinical course It seems probable that some patients simply do not report the symptoms to a physician when the disease is not particularly severe

The major reasons for delay in diagnosis were either failure to consider the possibility of thyroiditis or failure to palpate the thyroid gland The management of symptomatic treatment is relatively satisfactory Patients with mild cases may need only aspirin, but generally the more severe symptoms require specific medication, such as with adrenal steroids, or x-ray therapy The response to steroid therapy is dramatic

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VITAMIN A INTOXICATION AS A CAUSE OF PSEUDOTUMOR CEREBRI

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Three girls aged 14, 15, and 16 years had diplopia, papilledema, and other symptoms suggesting brain tumor In addition to various individual complaints, each had hypomenorrhea, alopecia, and rhagades or other marked forms of dermatosis They had been taking, respectively, 200,000, 200,000, and 90,000 units of vitamin A per day Treatment consisted in stopping the intake of vitamin A, in addition the oldest patient received acetazolamide as a diuretic The symptoms subsided rapidly, but in the oldest patient slight blurring of the margins of the optic disks were still present six months later Alopecia, rhagades, nonspecific dermatitis, migratory arthralgia, hepatosplenomegaly, and hypomenorrhea are important in the differential diagnosis between the pseudotumor cerebri of chronic vitamin A intoxication and true intracranial tumor

Pseudotumor cerebri is a syndrome of uncertain and probably multiple etiology It presents the picture of increased intracranial pressure with headache and papilledema Localizing neurological signs such as extraocular muscle palsies are most uncommon Complete neurosurgical diagnostic procedures are clearly indicated to rule out brain tumor, but their results are negative in pseudotumor cerebri The increased intracranial pressure is self limited, of some months' duration, and causes little damage, except that, in untreated severe cases, the patient may go blind from optic atrophy Although subtemporal decompression effectively reduces pressure, this surgical therapy has been superseded by acetazolamide (Diamox) therapy Acetazolamide, in doses of 500 mg twice daily, will ordinarily bring intracranial pressure within normal limits The highest incidence of pseudotumor cerebri is in adolescent or young adult females, usually those who are overweight[1]

Recognition of chronic vitamin A intoxication as a cause of the pseudotumor cerebri syndrome is im-

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From the Department of Ophthalmology University Hospital portant, because withdrawal of the excess vitamin A cures the patient, also expensive, uncomfortable, and hazardous neurosurgical diagnostic procedures may be avoided Diagnosis of chronic vitamin A intoxication is simple, providing the physician is aware of the syndrome In all cases of pseudotumor cerebri the patient and her family should be carefully questioned, as the vitamin administration may have been suggested by friends or a druggist and not prescribed by a physician After some months of daily ingestion of 100,000 units or more, the patient develops dryness, roughness, and desquamation of the skin, fissuring of the angles of the lips, loss of hair, migratory bone pain, hypomenorrhea, palpable enlargement of liver and spleen, and increased intracranial pressure Naturally, the presence of the findings and their severity is subject to considerable variation, depending on individual susceptibility and the amount of vitamin A intake A typical papilledema develops and is opthalmoscopically indistinguishable from the papilledema of brain tumor[2] Great emphasis must be placed on the fact that the papilledema may not disappear for from four to six months after vitamin A is discontinued Unless the physician realizes this, his confidence is shaken in advising against arteriographic and pneumoencephalographic examination Presumably, this persistence of papilledema is related to the large amounts of vitamin A that are stored in the liver

At times, large doses of vitamin A have been urged for skin, eye, renal, gynecologic, and ear disorders as well as the common cold The recommended daily requirement of vitamin A is 5,000 units in adults, increased to 6,000 units a day during pregnancy and 8,000 during lactation Vitamin A in large doses is prescribed most commonly by dermatologists for acne vulgaris, although such use rests on only empirical grounds Oliver[3] has suggested that if vitamin A is used at all in treatment of skin disease, a clinical trial should extend not more than two months, at a dosage which does not exceed 50,000 units daily, and labels on vitamin A products should include a warning of possible intoxication due to excess dosage Case histories of three patients with vitamin A intoxication follow

Report of Cases

Case 1 —A 14-year-old girl was admitted to Children's Hospital on Sept 11, 1956, with the chief complaint of leg pain of five weeks duration Two years prior to admission, the patient developed superficial nonpitting acne vulgaris, for which, 10 months prior to admission, 200,000 units of vitamin A daily had been prescribed by a dermatologist Two months prior to admission she had her last normal menstrual period, succeeding ones occurring at the normal interval but scanty and of one day's duration About the same time the patient noted scaling and cracking of her lips and fissuring at the corners of her mouth, for which she used a number of salves without success Five weeks before admission, she began complaining of dull constant pain in her legs, particularly about the knees, which was aggravated by activity At this time she was seen by her private physician, who directed that vitamin A be discontinued This advice was not heeded by the patient, unknown to either her family or the physician In the month prior to admission, leg pain worsened She walked with a noticeable limp, favoring her left leg, and was unable to continue in gymnastic activities at school She observed that her scalp hair became dry in texture and fell out in large quantities with brushing A maculopapular eruption on her trunk and desquamation of her palms and soles developed The family observed during this period that she manifested increasing irritability, but there were no specific symptoms of central nervous system involvement No bleeding or bruising was noted Appetite remained good, although the patient was on a self-imposed, rather rigid diet because of the acne

Family history was noncontributory The patient's own history was essentially unremarkable Menarche occurred two and one-half years prior to admission and menstrual periods had been normal up to the present illness

Physical Examination —Her weight was 54 kg (129 lb), height, 169 cm (5 ft 5 in), and blood pressure, 130/70 mm Hg The face was the site of superficial nonpitting acne vulgaris and milia The lips were scaled and cracked, and there were fissures at the corners of the mouth Over the trunk and, to a lesser degree, on the extremities was a fine discrete light-tan nonpruritic papular eruption The skin was dry, and the palms and soles were desquamating The underlying skin in these areas was delicate and thin Nikolsky's sign was absent The scalp hair was dry and loose and there was moderate alopecia The pubic and axillary hair was normal As seen in figure 1, the typical appearance of early papilledema was present in each eye The disk margins were completely blurred and slightly elevated, and the physiological depression was obscured Slight venous pulsation was present Minimal external pressure elicited venous collapse Fine capillary dilatation was apparent on the disk surface Glistening retinal edema encircled the disk, extending out about 1 disk diameter A number of fairly large and dense flame-shaped hemorrhages were clustered about the disk The macula lutea and periphery were completely normal There were no visual symptoms External ocular examination was entirely negative (Specifically, no exophthalmos or extraocular muscle paresis existed)

The liver and spleen were not enlarged Pain and tenderness existed in both legs, more in the left, particularly medial and inferior to the tibial tubercle There was no swelling, heat, or redness There was no weakness, sensory disturbance, or re-

Summary

An analysis of the recent experience with subacute thyroiditis at the Hitchcock Clinic shows that there is good reason to believe that the disease is more common than our statistics would indicate The diagnosis may be overlooked and the patient treated for pharyngitis, or some similar condition, while the thyroiditis runs its clinical course It seems probable that some patients simply do not report the symptoms to a physician when the disease is not particularly severe

The major reasons for delay in diagnosis were either failure to consider the possibility of thyroiditis or failure to palpate the thyroid gland The management of symptomatic treatment is relatively satisfactory Patients with mild cases may need only aspirin, but generally the more severe symptoms require specific medication, such as with adrenal steroids, or x-ray therapy The response to steroid therapy is dramatic

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VITAMIN A INTOXICATION AS A CAUSE OF PSEUDOTUMOR CEREBRI

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Three girls aged 14, 15, and 16 years had diplopia, papilledema, and other symptoms suggesting brain tumor In addition to various individual complaints, each had hypomenorrhea, alopecia, and rhagades or other marked forms of dermatosis They had been taking, respectively, 200,000, 200,000, and 90,000 units of vitamin A per day Treatment consisted in stopping the intake of vitamin A, in addition the oldest patient received acetazolamide as a diuretic The symptoms subsided rapidly, but in the oldest patient slight blurring of the margins of the optic disks were still present six months later Alopecia, rhagades, nonspecific dermatitis, migratory arthralgia, hepatosplenomegaly, and hypomenorrhea are important in the differential diagnosis between the pseudo tumor cerebri of chronic vitamin A intoxication and true intracranial tumor

Pseudotumor cerebri is a syndrome of uncertain and probably multiple etiology It presents the picture of increased intracranial pressure with headache and papilledema Localizing neurological signs such as extraocular muscle palsies are most uncommon Complete neurosurgical diagnostic procedures are clearly indicated to rule out brain tumor, but their results are negative in pseudotumor cerebri The increased intracranial pressure is self limited, of some months' duration, and causes little damage, except that, in untreated severe cases, the patient may go blind from optic atrophy Although subtemporal decompression effectively reduces pressure, this surgical therapy has been superseded by acetazolamide (Diamox) therapy Acetazolamide, in doses of 500 mg twice daily, will ordinarily bring intracranial pressure within normal limits The highest incidence of pseudotumor cerebri is in adolescent or young adult females, usually those who are overweight[1]

Recognition of chronic vitamin A intoxication as a cause of the pseudotumor cerebri syndrome is im-

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From the Department of Ophthalmology, University Hospital vulgaris The lips were scaled and cracked In the corners of the mouth, there were small fissures The skin was dry, and there was fine dry scaling over the forearms, hands, and feet Scalp and pubic hair were normal The optic disks bilaterally showed slight elevation with blurred margins The veins were slightly dilated and spontaneous venous pulsation was absent There was capillary dilation on the surface of the disk and a linear hemorrhage just off the disk of the left eye The retina surrounding the disk was glistening and edematous for from ½ to 1 disk diameter distance The macula lutea and periphery were normal The external eye examination was negative No abdominal organs were palpable No bone pain or tenderness was present

Laboratory Data —Hematocrit determination was 40%, white blood cell count, 4,300 per cubic millimeter, with a normal differential count, platelets, normal on smear, urine, normal on voided specimen, alkaline phosphatase level, 10 29 Bodansky units, electroencephalographic findings, normal, and fractional pneumoencephalographic findings, normal The bone survey included normal findings of chest, hands, and feet The skull showed minimal separation of the suture lines Lumbar puncture showed crystal-clear fluid, opening pressure was 50 to 70 mm H_2O (after pneumoencephalographic examination), with 21 lymphocytes per cubic millimeter and normal protein and sugar levels Visual fields showed enlarged blind spots

Course —On treatment with diuretics, the patient noted immediate improvement in visual complaints and lost seven pounds of weight Papilledema persisted unchanged for several months and then gradually decreased Slight blurring of the disk margins was still present on Aug 11, 1959

Case 3 —A 15-year-old girl, on May 15, 1958, noted some chapping of her arms, with cracking and peeling of her lips, as well as some ankle joint stiffness On the weekend of June 6, she slept continuously and was somnolent for the next two days On June 8, she had diplopia, and the next day she had headache, ringing in her ears, nausea, and anorexia She was examined by Dr J E Edwards of Lancaster, Ohio, on June 11, with findings of splenomegaly and bilateral papilledema He suspected vitamin A poisoning because of her somnolence, anorexia, and peeling of the skin, so inquiry was made as to the possible intake of this vitamin

It was learned that she had initially been given vitamin A, 50,000 units a day, by her druggist, which was later increased to 200,000 units per day by a dermatologist Her skin was reported to have cleared considerably with this therapy

Dr Edwards discontinued therapy with vitamin A and referred her to a local ophthalmologist who, because of the papilledema and retinal hemorrhages, wished her to have neurosurgical investigation By June 30, her appetite had improved and she was no longer sleepy or readily fatigued Diplopia persisted There had been no change in her menstrual periods When asked, her mother commented that hair had come out in handfuls on recent washing

On examination, there was found an alert, quiet girl of stated age who weighed 57 kg (125 lb) Her hair was soft, fine-textured, and markedly thinned on the forehead and over the ears There were pitted acne scars of the face, and the remainder of the skin was dry, scaly, and thickened She had bilateral papilledema, with scattered perivascular linear hemorrhages In the right retina there was a sharp white patch of exudate Cardiovascular examination was normal with a blood pressure of 120/80 mm Hg The spleen was palpable three fingerbreadths below the left costal margin, non-tender, and firm Neurological examination was normal, including angiographic and pneumoencephalographic examination

Her red blood cell count was 4,720,000, with a platelet count of 320,900 and a coagulation time of nine minutes The alkaline phosphatase level was 2 9 Bodansky units and acid phosphatase level 0 1 Shinowara-Jones-Reinhart units The serum calcium level was 10 0 mg , and the serum phosphorus level was 2 5 mg The carotene blood level was 38 8 (normal 10 to 20) Blue units per 100 ml Serum electrophoretic pattern was completely normal

The therapy consisted of stopping the vitamin A medication The diplopia disappeared on July 2, but the papilledema did not completely subside until Sept 9, 1958

Summary

Chronic vitamin A intoxication will produce a syndrome consistent with the diagnosis of pseudotumor cerebri Diagnosis is made by the associated presence of typical skin disorder, hair loss, hepatomegaly and splenomegaly, bone pain, somnolence, mental irritability, anorexia, diplopia, and hypomenorrhea Papilledema due to chronic vitamin A intoxication may require some months to disappear The use in skin diseases of vitamin A in large doses over many months is questioned, and any patient receiving such medication should be carefully observed for toxicity

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Doctor George Stine granted permission for the report of one case

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POSSIBILITY OF IATROGENIC FACTORS RESPONSIBLE FOR HYPERNATREMIA IN DEHYDRATED INFANTS

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and

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Current trends in the therapy of acute diarrheal disease in infants and children may be responsible for the reported increase in the incidence of hypernatremia In a series of 47 cases, 10 patients were found to have a serum sodium concentration of 150 mEq per liter or above These patients, mildly ill initially, became hypernatremic after receiving medical care as follows the prescription of abnormally large quantities of liquids with high salt content for oral ingestion (seven cases), the administration of isotonic sodium chloride solution by hypodermoclysis (two cases), or the intravenous administration of electrolyte solutions at too rapid a rate (two cases) The resulting hypernatremia produced coma in nine cases, convulsions in six cases, death in two cases, and persistent convulsive disorders in three cases

The reported incidence of hypernatremia in dehydrated infants has been increasing markedly in the past 10 years[1] Some of the authors have raised the question whether this increase is the result of certain new practices in the treatment of infantile diarrhea

Because this type of dehydration has such a high incidence of nervous system sequelae[2] it is important to know the reasons responsible for its increase It is imperative, therefore, that physicians have a high index of suspicion for this condition and be aware of its prevention, clinical features, and therapy

The purpose of this communication is to add to the evidence that there may be an improper type of therapy practiced by physicians which contributes to the problem[1] This will be done by presenting an analysis of a series of cases The conclusion we shall attempt to make plausible is that the administration of salt-containing fluids, either orally or parenterally, to an infant with dehydration must be done with caution

Method and Materials

During a two-year period from March 1, 1957, to March 1, 1959, there were 47 patients under 4 years of age who were admitted to the hospital with acute diarrheal disease Ten (21%) of these patients had hypernatremia with a sodium concentration of 150 mEq per liter or above Their clinical courses were studied as to age, duration of the present illness, feeding and fluid therapy prior to the recognition of hypernatremia, chemical analysis of the blood, clinical course, and therapy after the recognition of hypernatremia and complications (see table) Concentration of sodium and potassium in the serum were determined by flame photometry done with microquantities of serum (0 05 ml for sodium and 0 1 ml for potassium), chloride determinations were done by a microtitration method with use of mercuric nitrate with diphenyl carbazone as the indicator The carbon dioxide-combining power determinations were done with the Natelson Microgasometer and 0 03 ml of serum

Results

Six (60%) of these patients with hypernatremia had convulsions during their acute illnesses Hypertonic dehydration was accompanied by coma of varying duration in nine cases (90%) There were two deaths, a mortality of 20% Three infants (cases 1, 2, and 3 in table) were only moderately ill on admission to the hospital but became seriously ill and showed central nervous system signs after the administration of salt-containing fluids in dosages larger than those usually recommended

Three infants (cases 1, 4, and 6 in table) presented apparent sequelae In case 1, the onset of generalized seizures 11 months after recovery from the hypernatremic episode was reported These occurred four times in one month but did not recur during a subsequent year on anticonvulsant therapy The infant was six months slower than his twin in talking The onset of typical *petit mal* variant seizures within two weeks after discharge from the hospital was reported in case 4 These seizures persisted despite various forms of anticonvulsant therapy In case 6, the persistence of the same type of minor motor seizures which had characterized the acute hypernatremic episode was reported These seizures have been only partially controlled on trimethadione (Tridione) therapy

Comment

It is thought provoking to realize that most of the infants in this series were mildly ill initially and did not become seriously ill until they came under medical care Those who became seriously ill preceding hospitalization were those infants who became mildly dehydrated as a result of their diarrhea but who thereby became very thirsty and

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ingested large quantities of electrolyte-containing fluids that had been prescribed for them Probably the most commonly prescribed electrolyte-containing fluid for infants with diarrhea is milk, usually boiled and skimmed. It is not well appreciated that the ingestion of whole milk without supplemental water throughout the period of diarrheal losses will result in a hypertonic dehydration

The kidneys of healthy infants are capable of concentrating urine to only one-half the tonicity of adult urine [4] This handicap is further aggravated by dehydration states [5] The infant with diarrhea loses hypotonic fluid through the stool and through insensible loss from the lungs and skin If adequate amounts of hypertonic urine cannot be passed, because of immaturity or acute disease, his one efficient method for excreting excess solutes is lost The consequent elevation in the osmolarity of body fluids leads to a syndrome of hypertonic dehydration or hypernatremia

those to whom a high solute load was given parenterally It is common practice to give isotonic sodium chloride solution by hypodermoclysis to an infant who has mild diarrhea It is often not appreciated that this supplies 154 mEq of sodium chloride per liter, which is placed in a subcutaneous pool If the fluid administered subcutaneously differs markedly in composition and concentration from the extracellular fluid, it will attract water and possibly electrolytes from the extracellular fluids [8] Saline solution given subcutaneously may attract water from the extracellular compartment, producing a deficit which will lead to peripheral vascular collapse and shock

It also seems that rapidity of administration of fluid is important, in case 7 a low sodium-containing fluid (25 mEq of Na per liter) was administered rapidly (378 ml per kilogram of body weight per day) to a moderately lethargic dehydrated infant After 24 hours convulsions occurred, lasting 24 minutes, followed by a coma lasting 12 hours In contrast the patient in case 5, who was admitted with a serum sodium level of 201 mEq per liter, was given the same fluid slowly (180 ml per kilogram of body weight per day) The coma with which she had entered the hospital lasted only five hours, and she was spared convulsions

Data on Ten Cases of Hypernatremia

Case No	Age of Patient Mo	Duration of Illness Days	Chemical Analysis of Blood (mEq per Liter) Na	K	Cl	HCO_3	Feeding	Complications
1	5	2	170	4 2	130		Water and excessive amounts of Butler's solution given intravenously	Coma convulsions
2	8	2	167	2 1		6 75	Whole milk excess 0 9 isotonic sodium chloride solution given subcutaneously and excess amounts of Hartman's solution given intravenously	Coma convulsions died
3	10	3	156		99	12 0	Skim milk and 0 9 normal sodium chloride solution given subcutaneously	Coma
4	9	5	157	4 2			Large amounts of electrolyte containing fluid	Coma convulsions
5	8	2	201	3 8		4 5	Large amounts of electrolyte-containing fluid	Coma
6	6	3	158	8 1		15 0	Excessive amounts of Butler's solution given intravenously	Coma convulsions
7	1	3	164	6 4	99		Excessive amounts of Butler's solution given intravenously	Coma convulsions
8	8	3	165	8 6	110	10 0	Whole milk	Coma convulsions died
9	11	5	151		97	13 0	Skim milk	Meningismus
10	4	4	158	6 4		15 0	Skim milk	Coma

Since the baby with diarrheal disease has more ways of losing water than he has of excreting electrolytes, it is important that concentrated feeding mixtures not be used during the early treatment of diarrhea It has been pointed out by Pratt and Snyderman [6] that obligatory renal water loss is reduced if the load of electrolytes per calorie of feedings is reduced Colle and others [7] have pointed out the dangers of feeding high solute mixtures to patients with epidemic diarrhea

In a current popular therapy for diarrhea a commercially available electrolyte-containing fluid (Lytren) is used for oral ingestion It is sold as a powder and, when properly reconstituted with water, supplies 380 calories from a carbohydrate base, 50 mEq of sodium, 20 mEq of potassium, 4 mEq of sulfate, 30 mEq of chloride, 10 mEq of phosphate, and 4 mEq of lactate per liter The manufacturer warns that the sodium content of milk together with that of the electrolyte-containing fluid "might easily provide excesses of this ion This is illustrated in the present series (cases 4 and 5)

Those mildly dehydrated infants who became seriously ill after admission to the hospital are

The mortality and irreversible intracranial injury leading to chronic convulsive disorders are both related to vascular damage [2] Cooke [9] has theorized that the bleeding may be due to the tearing of bridging veins as water leaves the cells rapidly and engorges the perivascular space During the height of the hypernatremic episode, the patient is protected from seizures because of the effect of sodium ion in raising the membrane potential and increasing the electroshock threshold When therapy has been successful in lowering the sodium concentration, seizures occur as a result of vascular injury

The most commonly reported lesions [10] at autopsy were subdural effusions and meningeal hemorrhages The patient in case 8 in this series had a subdural effusion The brain of the other patient who died (case 2) was not examined

Summary

Hypernatremia complicated diarrheal disease in 21% of cases admitted to a pediatric service over a two-year period The mortality of hypertonic dehydration in this series was 20% Six of the 10 patients with hypernatremia convulsed during the acute episode Convulsive disorders persisted in three patients after recovery from hypernatremia High solute oral feedings or excessive amounts of intravenous electrolyte solutions, or both, played a possible etiological role in every case

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VALIDITY OF REPORTS OF PENICILLIN-RESISTANT GONOCOCCI

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A number of microorganisms can be confused easily with Neisseria gonorrhoeae, particularly the tribe Mimeae which was recognized and named in 1939 Mima polymorpha can cause not only urethritis but also fatal septicemia Some species of Mimeae are resistant to penicillin The evidence presented here shows that past reports of penicillin-resistant gonorrhea cannot be accepted because so many penicillin resistant organisms isolated from the genitourinary tract can mimic the gonococcus Studies of penicillin-resistant urethritis must include more thorough procedures for identifying the organisms involved The authors still consider penicillin in adequate dosage as the proper treatment for urethritis caused by Neisseria gonorrhoeae

Recently, publications have appeared which indicate that penicillin-resistant gonococci now constitute an important clinical and epidemiologic problem It is the purpose of this communication to critically review this evidence and to urge restraint and caution in accepting the concept of penicillin-resistant gonococci

Review of Literature

In 1939, DeBord [1] proposed the classification of a new tribe of bacteria, Mimeae, from the Greek meaning to imitate This is an apt name, because species of this tribe closely mimic species of the tribe Neisseriae and other gram-negative organisms both clinically and in the laboratory DeBord pointed out that species of this new tribe, particularly Mima polymorpha, might be mistaken for the gonococcus

In 1943, DeBord [2] published the laboratory observations of his clinical experience with this group of organisms This paper is of fundamental importance because it defined for the first time the spectrum of organisms which could be confused with Neisseria gonorrhoeae He demonstrated that, of 147 cultures from patients from whom organisms were isolated that were initially gram-negative diplococci on smear, almost one-third were Mimea and only 10 were N gonorrhoeae Forty-nine of his cultures

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…ant, Divisio[illegible] …ison Offic[illegible] (Dr DeY[illegible]in Gangarosa) and Bacteriologist (Miss … ment of B[illegible]iology, Walter Reed Army Institute of were from patients with vaginitis and only five of these were infections with N. gonorrhoeae. A list of organisms which can be confused with N. gonorrhoeae on gram stain as noted by DeBord includes Mima polymorpha, Herellea vaginicola, Colloides anowdana, Neisseria gigantea, Neisseria fulva, Neisseria intracellularis, and a small group of streptococci which tend to lose the gram stain. He noted in particular that M. polymorpha var. oxidans may easily be confused with N. gonorrhoeae, not only because of morphologic similarity on gram stain and culture but also because both give a positive oxidase reaction. He concluded, "As a result of this investigation it is felt that the identification of N. gonorrhoeae by smears is not justified."

In 1945, Deacon[3] isolated three strains of M. polymorpha from men with "therapy-resistant gonorrhea" and another from a patient with a chancroid lesion. These organisms were gram-negative diplococci and were oxidase positive. They were differentiated from Neisseria by biochemical and serologic methods. Recently, Ino and co-workers[4] reported on two patients with urethritis due to M. polymorpha var. oxidans who had a clinical syndrome which resembled gonorrhea.

In 1949, Faust and Hood[5] reported a case of fulminating septicemia resembling the Waterhouse-Friderichsen syndrome caused by M. polymorpha. This organism was confused with N. intracellularis because colonies typical of Neisseria, which gave a positive oxidase reaction, were seen. Differentiation was made by growing the isolated strain on plain agar at room temperature and noting its failure to ferment carbohydrates, thus ruling out N. intracellularis.

In 1953, Scott and Mahoney[6] pointed out that the number of isolations of Mimea is considerable in those laboratories in which attention has been called to the importance of these organisms. They also noted that some species of this tribe are resistant to penicillin as determined by the disk sensitivity method.

In 1954, Townsend, Hersey, and Wilson[7] reported on two patients with the Waterhouse-Friderichsen syndrome in whom M. polymorpha was the causative agent. The culture from one of these patients was sent to 13 different laboratories, all of which failed to identify it as M. polymorpha. Six laboratories identified the organism as a member of the genus Neisseria, three as Alcaligenes faecalis, one as Klebsiella, one as a gram-negative diplococcus, and two as an unidentified species. They concluded, "The lesson to be learned from these two cases is that M. polymorpha can on occasion cause a fatal septicemia and it can be easily confused with members of the Neisseria group."

Alarming reports from the armed forces at the end of World War II suggested that penicillin-resistant gonococcic infections were frequent among troops abroad. In 1946, Hughes and Carpenter[8] studied 216 men who were evacuated from the Pacific theater to the United States because of alleged penicillin-resistant gonorrhea. They found that 91% of these patients had urethritis due to some other bacteriological cause, including "unidentified small gram-negative bacilli," streptococci, and staphylococci. From 16 patients N. gonorrhoeae was successfully propagated. Only six of these strains were tested for penicillin sensitivity and were found to be inhibited by 0.08 units of penicillin or less. Fourteen of the 19 patients with gonococcic urethritis were treated with 300,000 units of calcium penicillin in peanut oil and beeswax and responded promptly. The five remaining patients, who failed to respond to 300,000 units of crystalline penicillin G in peanut oil and beeswax, were cured with an injection of 300,000 units of calcium penicillin in peanut oil and beeswax. The authors attributed the marked discrepancy between the observations in the Pacific theater and those carried out in the United States to faulty laboratory techniques. The few confirmed cases of gonorrhea were proved by history to be cases of reinfection. Many of the "unidentified small gram-negative bacilli" may have been species of the tribe Mimea.

A similar study was done by Cohn and co-workers[9] during the years 1946 to 1948. A total of 66 patients with alleged penicillin-resistant gonorrhea were studied in a special research clinic. None of these patients was found to have penicillin-resistant strains of N. gonorrhoeae. In 15 of them the bacteriological diagnosis could not be confirmed, but no comment was made as to what organisms were cultured from these patients. Of the remaining patients whose progress was followed all but three responded to a single injection of 300,000 units of penicillin. The remaining three patients required two or three treatments. These authors postulated that some persons with walled-off foci of infection not easily accessible to circulating penicillin may require larger doses or repeated injections of penicillin. Other alleged penicillin-resistant cases were explained by reinfection.

In a recent publication, Epstein[10] presented observations again supporting the concept of penicillin-resistant gonococci. This author treated 148 patients with cases of purulent urethritis among American military personnel stationed in Inchon, Korea, and found that 30 patients (20%) did not respond to ordinary doses of penicillin or had recurrences after an initial improvement. The diagnosis of gonorrhea was made by demonstrating gram-negative intracellular diplococci in stained smears of the urethral discharge, without bacteriological confirmation. This is the method which DeBord invalidated.

Cradock-Watson and co-workers,[11] Curtis and Wilkinson,[12] and Barile and others[13] have published data indicating that a significant proportion of recently isolated strains of N. gonorrhoeae are relatively resistant to penicillin by in vitro tests when compared to strains isolated in past years in other laboratories These authors have further shown that clinical relapses of purulent urethritis treated with penicillin could be correlated with strains of N gonorrhoeae which were more resistant to penicillin in vitro Reyn and co-workers[14] and Hirsch and Finland[15] have compared the susceptibility to penicillin of strains of N gonorrhoeae recently isolated with the susceptibility of strains of previous years Both groups showed a wider range of concentrations of penicillin susceptibility than was previously noted These concentrations are well within the therapeutic range or moderate doses of penicillin Although these studies suggest that there has been an increase in penicillin resistance on the part of some strains of N gonorrhoeae, there is not a single reference to the tribe Mimea in any of these publications, and it is not clear that species of this tribe were specifically excluded from these studies In personal communications, Cradock-Watson stated, "Species of the tribe Mimea were not specifically excluded in my work," and Reyn stated, "We have never been looking especially for these organisms (Mimeae)" Until a clinical laboratory study is done which specifically rules out other organisms, especially species of the tribe Mimea as the etiological agents in penicillin-resistant urethritis, we urge restraint in accepting as fact the concept of penicillin-resistant gonococci at this time

Laboratory Differentiation of the Most Common Organisms Appearing as Gram-Negative Intracellular Diplococci Involved in Purulent Urethritis

	Growth				Sugar Fermentation		
Organism	With 10% CO_2	In Air	On Meat Extract Agar	Oxidase Reaction	Dextrose	Maltose	Sucrose
N gonorrhoeae	+	−	−	+	+	−	−
M polymorpha var oxidans	+	+	+	+	−	−	−
M polymorpha	+	+	+	−	−	−	−
Herellea vaginicola	+	+	+	−	+	−	−

Penicillin remains the drug of choice for the treatment of gonococcic infections, but infections caused by the other organisms involved in purulent urethritis often respond better to the broad-spectrum antibiotics The table facilitates the laboratory differentiation of the more common species which we have found to be most easily confused with N gonorrhoeae A slide agglutination technique has also been developed which facilitates the rapid differentiation of M polymorpha and Herellea from Neisseria[16]

In view of the extensive evidence cited, demonstrating the rarity of penicillin-resistant gonococcic infection and the variety of penicillin-resistant organisms isolated from the genitourinary tract which can mimic the gonococcus, clinicians and laboratory workers are urged to explore the known alternative possibilities before rendering a diagnosis of "penicillin-resistant gonorrhea"

Summary

Penicillin in adequate dosage is still the drug of choice for the treatment of acute gonococcic urethritis Studies to date indicate that the range of susceptibility of strains of gonococci is well within the limits achieved with commonly used doses of penicillin Failure to respond to penicillin should suggest the presence of walled-off foci of infection or the presence of strains which require more than a single small dose of penicillin Some cases of purulent urethritis are due to species of the tribe Mimea which must be considered in the differential diagnosis The development of strains of Neisseria gonorrhoeae resistant to penicillin has not been proved

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TREATMENT OF EDEMATOUS EXTREMITY WITH DIURETICS

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This study concerned 56 patients with localized swelling in an upper or lower extremity occurring after thrombophlebitis, ulcer of the leg, radical mastectomy, trauma, or fracture There was no reason for believing that cardiorenal disease or hypoproteinemia contributed to the edema in these cases Appropriate local treatment was supplemented with diuretics, generally chlorothiazide, and restriction of oral salt intake All patients showed measurable decrease in their edema, and the response was good or excellent in all but six Particular advantage was found in the ambulatory management of ulcers of the leg The improvement of these edematous extremities by systemic therapy points to the likelihood of significant systemic factors in the symptomatology of these cases

The swollen extremity occurring after local trauma, surgery, thrombophlebitis, and other presumably local "surgical" disease continues to present a serious therapeutic challenge Elevation, local compression, and removal of incompetent veins have all been predicated on the thesis that abnormal vascular drainage leads to an increase in capillary pressure and hence of capillary transudation This concept, derived from Starling's law and first stated by Virchow, has provided a simple mechanical concept that has dominated thinking in these conditions

There are, of course, a number of other possible explanations for the phenomenon of the swollen limb The availability of orally given diuretics that can be safely and conveniently administered over long periods of time has made for remarkable progress in the treatment of the edema of cardiac failure, hypoproteinemia, renal disease, the toxemias of pregnancy, and premenstrual retention of water The incidence and degree of edema in localized diseases is not proportional to the degree of trauma, venous incompetency or obstruction, or other pathological change, in general, it tends to be more severe in women and in older persons, two groups which are known to have more difficulty with retention of salt and water This is an account of the use of salt restriction and diuretics in patients with swelling of an extremity not associated with obvious systemic disease

In 1924 Fay[1] published a clinical study which established the place of diuretics and restriction of salt in the treatment of cerebral edema occurring after trauma He started a continuing trend away from the extraordinary abuses of salt therapy in general surgical management Lapp and Neuffer (1930)[2] advocated a rice and salt diet for the treatment of crural ulcers, infections, and trauma of the lower extremities DeTakats (1933)[3] described favorable effects from this diet and the use of diuretics in the management of the edema of thrombophlebitis, he also has mentioned his recent use of chlorothiazide in therapy of patients in the postphlebitic state[4]

Materials and Methods

This report is based on observations of 56 patients, history and physical examination established an obvious local basis for the swelling of the involved extremity While some of these patients had hypertension and others were known to have some arteriosclerotic heart disease, only one with an ulcer of the leg had ever received digitalis, and none showed evidence of cardiorenal failure by the usual diagnostic criteria Determination of the serum proteins was occasionally made, and the findings were uniformly normal

A general classified summary of the series is presented in table 1 The patients with thrombophlebitis, ulcers of the leg, and lymphedema of the arm after radical mastectomy for carcinoma of the breast had long-standing illnesses The edema occurring after fractures is generally transient, and the patients included in this study were, therefore, those that had persistent edema Those listed with trauma had acute injury and incapacitating swelling These cases included contusions and hematomas or lacerations in a leg or foot, sometimes associated with varying degrees of infection

Conventional treatment appropriate for the specific condition was supplemented with diuretics and dietary salt limitation Chlorothiazide (Diuril) in doses of 1 to 2 Gm a day was used in all cases but was sometimes supplemented with meralluride (Mercuhydrin) sodium administered intramuscularly In some patients intake of salt was quite high, whereas in others little change in their habits was required to obviate any obvious excesses In such chronic conditions, a diet of rice might have proved more of a nuisance than the disease and it was not attempted Anorexia and dizziness required temporary cessation of drug therapy in some patients,

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From the departments of surgery Vassar Brothers Hospital and St Francis Hospital and in one allergic person a generalized skin eruption, probably not related to chlorothiazide, prompted discontinuance of all drug therapy While some of these patients were hospitalized from time to time, all were ambulatory during the period of these observations

TABLE 1 —*General Classification of Patients*

Condition	Patients, No	Age, Range	Age Average	Sex Ratio Men Women	Duration of Treatment Wk
Thrombophlebitis	15	30-78	58	9 6	5
Ulcers of leg	14	47 83	63	7 7	12
Trauma	9	27 81	46	5 4	2
Mastectomy	6	27 70	52	0 6	7
Fractures	12	30 80	59	2 10	8
Totals	56	27 83	57	23 33	7

The presence of casts, open wounds, or infections sometimes limited observations, but, wherever feasible, principal reliance was placed on measurement of the displacement of water by the diseased extremity Determination of body weight, circumferential measurements, and inspection do not provide the precise accounting permitted by the principle of Archimedes

Results

All patients showed measurable and reversible improvement in the size of their involved extremities with this program (table 2) The results are tabulated in table 2—poor showing little change effected only with continued high dosage of chlorothiazide, good definite improvement making continued therapy worthwhile, and excellent essentially complete disappearance of edema or marked improvement in the course of the disease or both Drops in body weight of 15 lbs (7 kg) were not unusual in patients with massive edema Losses in a given extremity, as measured by the displacement of water in a container 12 in high, varied from 1 to 14 kg The limited height of the container was ideal for the lower extremities, but this possibly contributed to the poor results in conditions such as lymphedema of the arm in which maximal swelling generally occurs at or above the elbow

The most gratifying response occurred with the thrombophlebitic group in which the tightness, eczema, or weeping of the skin was readily relieved, the majority of these patients have been maintained with dietary control and occasional diuresis Dramatic improvement in patients with long-standing ulcers of the leg occurred sometimes in weeks, but these measures are certainly no substitute for classic therapy or for enduring care in the handling of these limbs The short duration of treatment used in cases of trauma made it apparent that evaluation of this group was much less controlled than in the chronic disease classifications Results in the mastectomy group were almost uniformly disappointing

Report of Cases

CASE 1 —A 63-year-old woman had had swelling discoloration, and itching of her legs with intermittent ulceration for 30 years She used large amounts of alkali, principally soda bicarbonate, for relief of constipation and upper gastrointestinal distress She gave a history of receiving hormone injections every two weeks for 20 years to minimize the effects of her menopause Examination showed an obese woman with a blood pressure of 200/90 mm Hg but no definite evidence of cardiac disability There were irregular ulcerations of both legs and scarring and pigmentation of the skin of the ankles She was placed on a limited sodium intake and diuretics Pressure bandages were continued with petrolatum dressings Despite continued ambulation, healing of her ulcers occurred in a month's time, and with healing there was a considerable reduction in the amounts of diuretic needed

CASE 2 —A 47-year-old carpenter had had an appendectomy 23 years before, complicated by the development of thrombophlebitis and pulmonary embolism for which he was treated with a vein ligation in the calf, four subsequent operations for the removal of veins in both legs, numerous local operations for persistent ulcerations, and lumbar sympathectomy His diet included large amounts of salt with his food

Examination showed no significant superficial veins in his lower extremities, there were numerous extensive scars and large ulcerations over both medial malleoli He was treated with rest in bed for nine days and then placed on a low salt diet and regular injections of meralluride and later chlorothiazide, 2 Gm daily He continued to use pressure dressings as he had for many years He has had variable stasis eczema at times, but, at the time of this writing, had remained free of ulcerations for a longer period than at any time since his appendectomy

CASE 3 —A 30-year-old factory engineer incurred a long, oblique fracture of the right humerus which was treated with a hanging cast Ten days after the application of the cast, massive swelling of the hand was apparent, a new cast was applied because of the possibility that there was some pressure on his arm, but this failed to relieve his swelling Treatment with chlorothiazide, 1 Gm daily, relieved his swelling, and discontinuance of chlorothiazide resulted in recurrence of swelling, which was again

TABLE 2 —*Summary of Results of Treatment*

Condition	Patients, No	Result		
		Excellent	Good	Poor
Thrombophlebitis	15	9	5	1
Ulcers of leg	14	8	6	0
Trauma	9	5	3	1
Mastectomy	6	1	3	2
Fractures	12	3	7	2
Totals	56	26	24	6

controlled with diuretics Nine weeks after his injury, swelling had disappeared and did not recur after the discontinuance of therapy with chlorothiazide

Case 4—An obese, 45-year-old housewife had a left radical mastectomy, postoperatively she did well, and full function promptly returned to the arm despite the appearance of some swelling of the arm two weeks after her operation Limitation of salt and the use of diuretics produced some reduction of her edema, but a persistent effort was not made Nine months later, because of menorrhagia associated with fibroids, hysterectomy and salpingo-oophorectomy were performed, and there was prompt and complete disappearance of edema in the left arm There was gradual return of edema in the arm in the succeeding months which did not equal that present previously and which was more responsive to treatment

Comment

While the swelling in the extremities of these patients uniformly showed some response to intensive treatment with diuretics and restriction of salt intake, this response was sometimes unsatisfactory, and it is not intended to present this therapeutic regime as a total treatment for these frequently complicated and difficult cases

It should be equally apparent that total reliance on mechanical explanations for the swelling of the extremities is also inadequate and that new approaches to them are desperately needed Many patients with large, quite incompetent veins have no swelling, eczema, or ulceration of their legs In those with ulceration, even the most radical attack on incompetent veins leaves the patient with a leg that requires special care for life to prevent recurrent ulceration Better recognition is now being given to the fact that uncomplicated varicose veins are strictly a cosmetic problem, and, at the least, thrombophlebitis must have been present to permit the development of ulceration[5]

When a basis for implicating the venous system in these patients has been lacking, theoretic reliance has been placed upon presumed lymphatic vessel obstruction Arnulf[6] has published a series of papers describing normal lymphographic findings in the chronically swollen leg and even the development of excellent lymphatic collaterals in the so-called lymphedema that occurs after radical mastectomy

Clearly all the answers are not known, and, on a local level, the arteriole and capillary offer obvious possibilities This report suggests that in the absence of obvious cardiac, renal, or metabolic disease, large stores of fluid in the body are available for local accumulation and that this process can be limited by means that presumably have only systemic effects The explanation for the fact that one person will have swelling while another with disease evidently as severe will not may be on a metabolic rather than a local basis It is probably not just chance that the average age of these patients was 57 years While most of the women in the series were postmenopausal, those that were not uniformly noted increases in their edema prior to their menses Case 4 illustrates dramatic improvement after oophorectomy in a swollen arm that had developed after radical mastectomy

A word of caution is indicated in recommending long-term use of new drugs in chronic disease In this series therapy with high dosages was discontinued in those patients who responded poorly to therapy, in the others, improvement of the inflammatory complications of their disease uniformly permitted intermittent dosage after a period of weeks Particular care is required in the treatment of patients with renal disease and uremia, which may become greatly increased by the use of chlorothiazide In the prevention of hypopotassemia, limitation of sodium intake is as important as the provision of adequate potassium, some recent experiments by Edmonds and Wilson[7] do much to explain this physiological facet

Summary

Experience with the use of restriction of salt and diuretics given orally was favorable in a series of 56 patients, all of whom had persistent swelling of one or more extremities and peripheral disease adequate to account for this enlargement The success of the treatment suggests that systemic factors play a significant role in these cases and that these factors should be considered in therapy

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SUPPRESSION OF LACTATION

USE OF A FLUOXYMESTERONE–ETHINYL ESTRADIOL COMBINATION

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The use of hormonal preparations for the control of postpartum breast symptoms is advisable In this study of 118 maternity patients, a new androgen-estrogen combination tablet was administered to 75, while 43 received placebo tablets The androgen estrogen combination, given at three dosage levels, was effective without significant side effects Those patients who received the highest dosage experienced the most marked relief of breast pain, engorgement, and lactation and showed the least need of additional supportive measures

The widespread tendency toward breast feeding by the obstetric patient is well known to all obstetricians Ever since the advent of sex steroid therapy for suppression of lactation, the literature has abounded with reports of various preparations for control of the frequently annoying symptoms that are associated with postpartum initiation of lactation Gold and Cohen [1] in an excellent review of the literature have recently pointed out that consistently good results have been obtained with estrogens alone, progesterone alone, androgens alone, estrogen-progesterone combinations, and estrogen-androgen combinations However, they also pointed to the consistent presence of a small number of patients who have experienced rebound phenomena or undesirable side-effects, all of which indicate that the ideal suppressant for 100% of patients is yet to be found

In a previous report [2] the authors showed the efficacy of fluoxymesterone in the control of lactation and the postpartum breast symptoms associated with it The almost complete absence of rebound problems and other side-effects, together with adequate control of pain, engorgement, and lactation, indicated that this drug is as effective as, and perhaps better than, most of the other sex steroids However, a dose of at least 5 0 mg twice a day and preferably three times daily was necessary for adequate control Here, as in other reported studies, there was still a small group of patients who experienced difficulty

Since the effectiveness of fluoxymesterone alone has been proved, we decided to undertake further studies to evaluate it when combined with small dosages of ethinyl estradiol Such a preparation would have the advantage of lower doses of androgenic substance with the addition of less expensive estrogens and yet have enough antiestrogen effect to inhibit secondary problems such as withdrawal bleeding Fluoxymesterone is a halogenated androgen which is the most potent orally given active androgen commercially available Ethinyl estradiol is an orally given active synthetic derivative of the natural ovarian follicular hormone, estradiol It possesses estrogenic potency surpassing that of any known orally given estrogen available for clinical use Because of its high potency, a very small amount is required to elicit a typical estrogen effect The structural formula of each of these drugs is depicted in figures 1 and 2

Katzman [3] determined that an ideal androgen estrogen ratio for control of breast symptoms is 20 to 1 when given intramuscularly The preparation used in the present study consisted of 1 0 mg of fluoxymesterone combined with 0 02 mg of ethinyl estradiol, a ratio of 50 to 1 on a weight basis This difference has been based on observations that orally given fluoxymesterone is about equal in potency to intramuscularly given testosterone propionate and that orally given ethinyl estradiol is up to two and one-half times more potent than estradiol given by injection Since each of these ingredients has already been proved to be of value in lactation control,[4] it did not seem necessary to undertake a double-blind study to determine whether the combination would be effective The actual purpose of the investigation was to determine, first, the optimum dose for control, and, second, whether there was any substantial difference in the combination than with the androgenic component alone

Methods and Materials

This study was conducted with 118 maternity patients on the private and ward services at the Methodist Episcopal Hospital in Philadelphia The cases were divided into four groups Group 1 consisted of ward patients and these were used as the control group There were a total of 43 patients in this group, and all received only placebo tablets

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Group 2 consisted of 25 patients, they received one tablet of the preparation daily Group 3 consisted of 26 patients receiving one tablet twice daily, and group 4 was comprised of 24 patients who received one tablet three times a day The latter three groups were all private patients, but the dosage was administered on a strict alternating basis with no attempt to select patients for a given regimen

None of the patients in any of the four groups were permitted the use of breast binders, ice bags, fluid restriction, or analgesics unless specifically ordered by the resident or attending physician, but a good supporting brassiere was allowed if the patient so desired All patients were questioned and examined daily by attending and resident staff, and notes were kept regarding pain in the breasts, engorgement, temperature elevation, lactation, and whether additional measures were required for the alleviation of discomfort Patients were also questioned and examined for evidence of side-effects such as virilization and abnormal amounts of bleeding Therapy was started as soon after delivery as the patient could tolerate fluids by mouth and was continued daily until the time of discharge from the hospital, but not longer than the sixth postpartum day

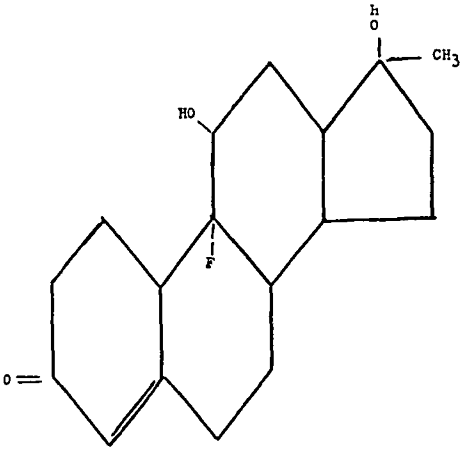

Fig 1 —Structural formula of fluoxymesterone

Within one month of the time of discharge all patients were mailed a questionnaire with a self-addressed and stamped envelope to be returned after the completion of the first menstrual period Information requested on this card consisted of date of the first menstrual period, evidence of secondary filling of the breasts, presence or absence of vaginal bleeding, and a request for comments on any other disorders of the breast that may have arisen

Results

In this study we found that the number of patients in any group experiencing breast symptoms on the day of delivery or the first postpartum day was statistically insignificant Likewise, no significant conclusions could be drawn after the fifth postpartum day, since all patients were either symptom-free or had been discharged from the hospital by that time The actual evaluations, therefore, were centered on the second, third, fourth, and fifth days We believe that the best criteria for success or failure of any lactation suppressant are the presence or absence of breast pain, engorgement, lactation, and the necessity of additional measures for control, these then were taken as yardsticks by which to measure the effectiveness of the preparation

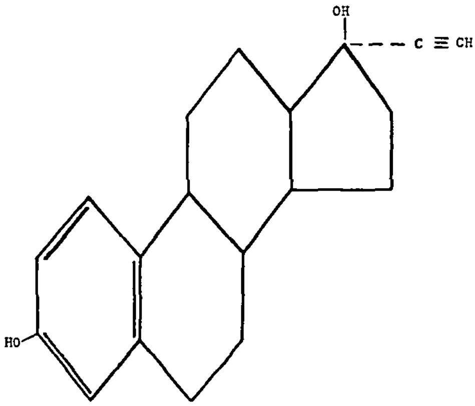

Fig 2 —Structural formula of ethinyl estradiol

Pain in the Breasts—Breast pain was found most commonly in the control group receiving placebos (fig 3) It is interesting to note that on the second day there was actually less pain in this group than in any group receiving the hormonal therapy, with only 13 9% of patients complaining of pain However, by the third day the incidence rose to 46 5% and thereafter the control group displayed a consistently greater incidence of pain than any other

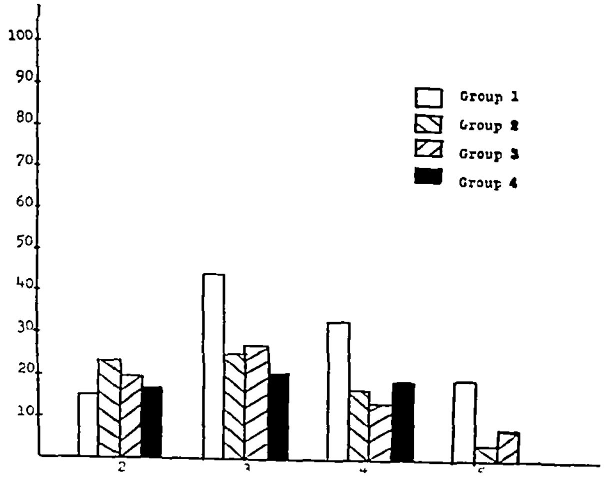

Fig 3 —Pain in breast, horizontal axis days, vertical axis % of patients

group Breast pain in group 2, receiving one tablet daily, averaged 17% throughout the four-day period, and in group 3, receiving two tablets daily, averaged 16 3% for the same time When the dosage was increased to three tablets daily (group 4), the mean percentage of pain dropped to 13, with no patients experiencing pain by the fifth postpartum day Thus, taking pain as a criterion, the optimum dosage would be one tablet of this preparation three times a day These figures compare favorably with those of Morton and Miller,[5] who also detected 85 to 93% control in hospital patients with increased doses of stilbestrol, and they are slightly better than those of Garry[6] who obtained 83% relief with an orally given estrogen-androgen combination

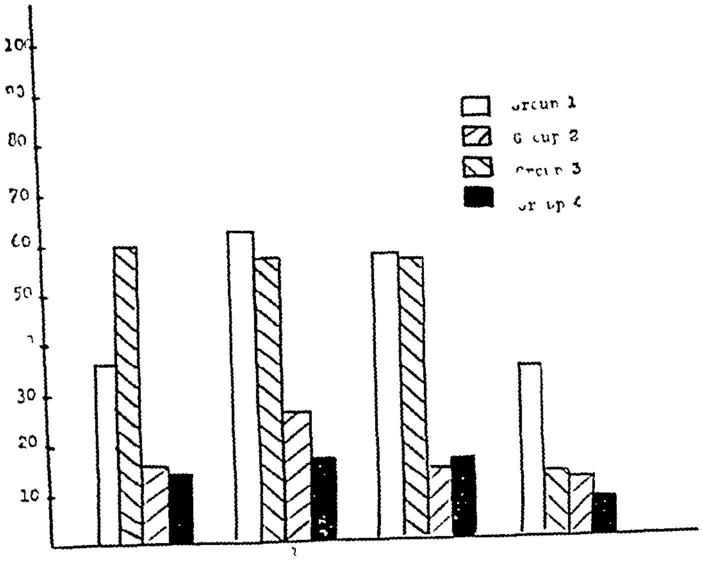

Fig 4 —Engorgement, horizontal axis days, vertical axis % of patients

Engorgement—Determination of engorgement was made by the attending and resident physicians by daily palpation of the breasts Figure 4 shows the results in the four groups with regard to this finding It can be seen that the control group experienced filling of the breasts in more than one-half of the cases, rising to 62 8% on the third postpartum day, and averaging 48 3% Group 2 patients also experienced substantial engorgement, with a mean of 46 6% for the entire period However, when the dosage was increased to twice a day (group 3), the mean percentage of engorgement dropped to 17 2, with a high of 26 9% on the third day When the dosage was increased to three times a day (group 4), the mean percentage decreased to 13 5, with a high of 16 7% on the third and fourth days Taking engorgement alone as a criterion, the optimum dosage is again found to be one tablet three times daily

Lactation—Lactation is both a subjective and an objective means of measuring the degree of success, and figure 5 depicts the results of this finding This complaint was not as prevalent in any group as were those of a more subjective nature Nevertheless, a mean 32 5% of the control group displayed secretions from the breasts Those in group 2 had a mean incidence of 18 0%, a substantial decrease from the control group The average percentage of lactation in the group 3 patients was 10 5, and the average for group 4 was 13 5%, indicating that there is little difference in dose required for the suppression of the actual secretion from the mammary gland These findings, perhaps more than any others, show the definite advantage of the use of hormonal preparations in the control of postpartum breast symptoms over the regimens that call for only supportive measures without hormones

Figure 5 also lists the presence of lactation in the postpartum state This information was determined from the follow-up questionnaire sent to all patients Fifty-five of the patients (47 0%) returned cards as requested None of the replies indicated complaints of secondary pain or engorgement, but a few patients did complain of secondary or persistent lactation after discharge It can be seen that 6 9% of the control patients experienced this, and all of these patients stated that further therapy was necessary after discharge The symptoms lasted from two to four weeks Groups 2 and 3 were almost equal in incidence of symptoms, with 12 0% and 11 5% respectively In general, the complaints were not as severe in these groups as in the control group Of the group 4 patients, only one (4 2%) experienced difficulty after discharge from the hospital

Other Measures—A fourth measurement of the efficacy of this drug was compiled with use of the number and percentage of patients requiring therapy in addition to the hormonal product itself Such measures included the use of analgesics, ice bags, binders, and fluid restriction for symptomatic relief As stated before, these were reserved only for the patients who developed symptoms not controlled by the hormonal preparation, and, when additional measures were ordered, records were kept as to the methods used and the number of days required Figure 6 shows the number of patients requiring additional measures of one or more types to allev

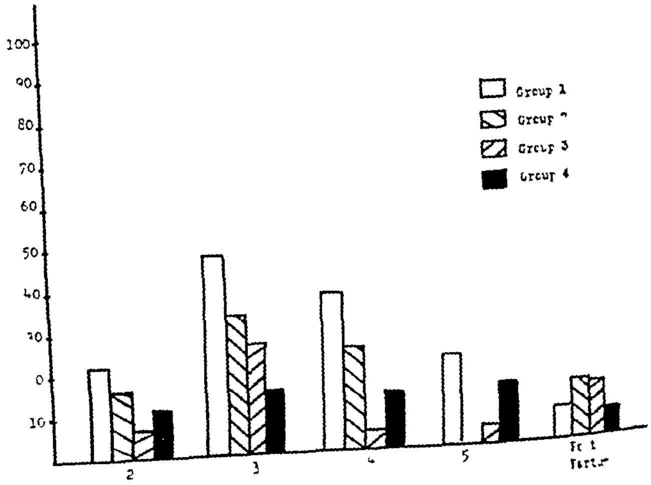

Fig 5 —Lactation, horizontal axis days, vertical axis % of patients

ate any symptoms or findings One can see that there was a general decrease in the necessity for such measures with the increase in dosage of hormone As might be expected, the third and fourth days showed the highest incidence, with those patients who received only placebos experiencing the greatest need The mean requirement for group 1 was 30 3%, the mean for group 2 was 21 0%, for group 3 it was 18 2%, and for group 4, 13 5% Thus, with regard to the requirements for additional measures, the advantage of increased doses is evident

The final means of analysis of the efficiency of this drug was done by means of the postpartum questionnaire cards, which were returned by 47 0% of patients after the completion of the first menstrual period, usually within six weeks of the time of delivery The findings of recurrent lactation in this survey have already been indicated Other items requested failed to disclose any untoward findings There was no evidence of masculinization, nor was there any particular delay in the onset of the first menstrual period No patient experienced withdrawal bleeding

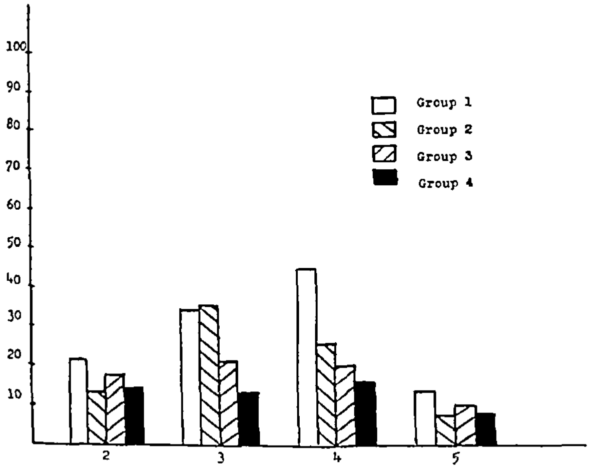

Fig 6 —Analgesics, binders, ice bags, and other measures, horizontal axis days, vertical axis % of patients

Comment

The suppression of lactation has been undertaken by many various methods in the past, both hormonal and nonhormonal The present study again indicates that the use of hormones is indeed desirable for the suppression of lactation and that patients are more comfortable with less annoying symptoms when so treated From the reports in the literature[7] and from our own experience[2] we have concluded that most hormones, regardless of type, will give satisfactory results The present study substantiates this The trend can be seen in progressive dosage forms and would seem to indicate that a sufficiently high titer of the hormone is necessary to suppress adequately the lactogenic hormone from the anterior pituitary gland

The efficacy of fluoxymesterone alone has been shown[2] The addition of small amounts of ethinyl estradiol allows for a decrease in the amount of androgenic substance and a resultant decrease in cost, yet allows for adequate control of the annoying symptoms associated with postpartum initiation of lactation Withdrawal bleeding, so frequently encountered with the use of estrogens alone, was not detected in this series, a finding which we believe to be of definite advantage The presence of a small percentage of patients with secondary or persistent lactation indicates that the ideal suppressant for 100% of cases has still not yet been found Nevertheless, this combination androgen-estrogen preparation is a valuable tool in the management of the postpartum patient

Summary

One hundred and eighteen patients have been studied with regard to the ability of a fluoxymesterone-ethinyl estradiol combination to suppress lactation in the immediate puerperium Three groups of patients were given different dosage regimens and a fourth group was used as a control, comparisons were made with regard to the presence or absence of breast pain, engorgement, lactation, and the requirements for additional supportive measures

The optimum dosage was determined to be one tablet three times daily, beginning as soon after delivery as the patient can tolerate fluids by mouth and continuing until the time of discharge No side-effects, withdrawal bleeding, or virilization were noted in any patient either during the period of administration or after discharge from the hospital as determined by follow-up correspondence with the patients This combination, when given in adequate dosage, is an effective and safe means of controlling postpartum lactation symptoms

2400 S 21st St (45) (Dr Bare)

Documentation of private patients in this study was allowed through the cooperation of the attending staff members under the supervision of Dr George A Hahn

The fluoxymesterone-ethinyl estradiol combination (Halodrin) was supplied by the Upjohn Company, Kalamazoo, Mich

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MENINGITIS FOLLOWING TRAUMA TO THE HEAD AND FACE

Emanuel Appelbaum, M D, New York

The seriousness of infections complicating injuries to the head and face prompted a study of 91 cases of post-traumatic meningitis While all the injuries were severe, definite evidence of fracture of the skull or nose was noted in only 48 instances In this series, the interval between the trauma and the development of meningitis ranged from several hours to five years In addition to the typical symptomatology of meningitis, noted in all the patients, there were 15 instances of rhinorrhea or otorrhea and 13 cases with bleeding from the ears or nose The pneumococcus was the etiologic agent in 47 instances and various other organisms were found in the remaining cases The low recovery rate of 5 among 42 patients in the prechemotherapeutic era contrasted sharply with a recovery of 18 among 20 patients on antibiotic therapy The occurrence of repeated bouts of meningitis in three patients was a disturbing problem

It is well recognized at present that injuries to the head and face, especially those occurring in industrial and traffic accidents, represent an important health problem The seriousness of the problem is magnified when these injuries are complicated by infections of the brain, spinal cord, or meninges It is the purpose of this communication to present a study of 91 cases of post-traumatic meningitis, seen by the Division of Acute Infections of the Central Nervous System of the New York City Department of Health, before and after the introduction of chemical and antibiotic therapy

Clinical Aspects

Nature of the Trauma—Table 1 shows the type of trauma observed in this series of 91 cases While fracture of the skull or nose is listed in only 48 instances, it is a reasonable assumption that a fracture was present in many, if not in most, of the other cases It may be pointed out that the diagnosis of fracture was based either on definite clinical evidence or on roentgenographic, operative, or postmortem findings In two cases of head injury a brain abscess developed, as a result of extension of a frontal sinus infection in one instance and the probable spread of such an infection in the other Meningitis followed operative intervention eight months after the injury in the first case and spontaneous rupture of the abscess six weeks after the trauma in the other

Interval Between Trauma and Development of Meningitis—In this series of cases the time that elapsed between the injury and the onset of meningitis was determined in 83 instances, as shown in table 2 It may be noted that in 10 instances the interval was less than 24 hours and in one it was five years In the majority of the cases meningitis occurred within two weeks of the trauma

Age and Sex Distribution—Table 3 shows the age distribution of the patients in this series The youngest patient was 6 months and the oldest 65 years of age The wide range in age and the high incidence among young children are evident The series comprises 79 male and 12 female patients This would seem to indicate that male patients are more frequently exposed to hazards

Symptomatology—The patients presented the typical picture of meningitis Individual patients showed considerable variation in the severity of the disease, but most appeared critically ill The salient signs and symptoms are shown in table 4 These are indicative of diffuse involvement of the central nervous system Certain symptoms, such as headache, are often difficult to elicit because of the patient's age or mental state Signs of meningeal irritation and a change in sensorium were almost uniformly present However, a clear mental state was noted in three patients The cranial nerves most often involved were the second, third, sixth, and seventh Paresis or paralysis of extremities was encountered in three cases Bulging of the fontanel was an early sign in infants Changes in the reflexes were frequently noted The fundi often showed congestion of the disks and, on occasion, papilledema It may be seen from table 4 that the important symptoms of bleeding from the nose or ears and cerebrospinal fluid rhinorrhea or otorrhea were not nearly as frequent as is generally expected

Pertinent Laboratory Data

Cerebrospinal Fluid Findings—Most of the spinal fluids showed varying grades of cloudiness and some were purulent Seventeen of the fluids were xanthochromic and five were bloody All the initial fluids showed pleocytosis, ranging from 210 to 11,000 cells per cubic millimeter, with a predominance of polymorphonuclear cells The protein ranged between 23 and 809 mg per 100 cc In the vast majority of the cases the protein content was moderately or markedly increased The spinal fluid sugar content ranged from less than 10 to 75 mg per 100 cc but was below 40 mg in 79 of the cases The

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From the Bureau of Laboratories, Department of Health

Read before the 87th annual meeting of the American Public Health Association in Atlantic City Oct 21 1959 diagnosis was confirmed bacteriologically in the 91 cases by recovering organisms from the spinal fluid culture in 85 instances and by positive smears in 6 cases The latter were further confirmed by a positive quellung reaction or the presence of a positive blood culture The distribution of the causative organisms is shown in table 5

TABLE 1—*Types of Head and Face Trauma in Ninety-one Cases of Post-Traumatic Meningitis*

Type of Trauma	No of Cases
Fractured skull or nose	48
Blow on head or striking head in fall or automobile accident	22
Injury to head or face (type unspecified)	10
Penetrating injury (bullet or stab)	9
Dog bite on face	1
Burn on upper part of neck	1
Total	91

Blood Studies—Blood cultures were done in 39 cases Of these, 13 were positive (pneumococcus 11, hemolytic streptococcus 1, staphylococcus 1) and 26 were negative

In the majority of the cases the white blood cell count showed leukocytosis, ranging between 20,000 and 40,000 cells, with 85 to 95% polymorphonuclear cells The highest white blood cell count was 47,000 and the lowest 8,000

Roentgenograms of the Skull and Nose—Roentgenographic records were available in 45 cases Of these, 26 revealed evidence of fracture, one showed osteomyelitis, and one the presence of a bullet In one of the patients with brain abscess the roentgenogram showed a defect in the right frontal bone, and the ventriculogram showed a shift of the ventricles to the left Among the 16 cases with normal roentgenograms, the presence of skull fracture was demonstrated at operation in three cases and at postmortem examination in four instances Pneumocephalus, which is conclusive roentgenologic evidence of dural tearing, was not recorded in this series

TABLE 2—*Interval Between Injury and Development of Meningitis in Ninety-one Cases*

	No of Cases
Unknown	8
<1 day	10
1 day to 1 wk	37
1 to 2 wk	8
2 wk to 1 mo	6
1 to 2 mo	6
2 to 6 mo	8
6 mo to 1 yr	2
1 to 2 yr	5
5 yr	1
Total	91

Outcome, Complications, and Autopsy Data

Outcome—Table 6 shows the therapeutic regimens and the results Among the five recoveries in the prechemotherapy period were two cases of influenzal meningitis that were treated with specific antiserum Three patients with streptococcal meningitis recovered without the use of any specific measures The improved results following the introduction of sulfonamides and the high recovery rate obtained with antibiotics are obvious

TABLE 3—*Age Distribution in Ninety-one Cases of Post-Traumatic Meningitis*

Age Yr	No of Cases
<1	3
1 to 10	40
11 to 20	8
21 to 30	11
31 to 40	11
41 to 50	10
51 to 60	5
>60	3
Total	91

Complications—In 21 of the cases the meningitis was associated with serious complications There were four instances of pneumonia Varying grades of deafness occurred in five patients, in one of whom there was also postoperative anosmia, which subsequently improved Purulent otitis, with or without mastoiditis, was noted in four cases Orbital cellulitis preceded the meningitis in one patient and developed during the course of the disease in another Purulent arthritis was noted in one case, in which there was also bacteremia One patient developed unilateral optic atrophy There was one instance of a complicating subdural abscess, which required surgical intervention Marked muscular spasticity and mental retardation were serious residua in one case However, these complications had been noted prior to the onset of the meningitis and were attributed mainly to the brain damage which resulted from the trauma There were two instances of brain abscess, both of which preceded the onset of the meningitis

Recurrence of Meningitis—In this series there were three instances of recurrent meningeal infections The data on these three patients are shown in table 7 It may be noted that each of these three cases was associated with fractured skull and persistent cerebrospinal fluid rhinorrhea Complete recovery followed the use of sulfonamides in one and antibiotic treatment combined with surgical repair

TABLE 4—*Salient Signs and Symptoms in Ninety-one Cases of Post-Traumatic Meningitis*

	No of Cases
Headache	58
Vomiting	62
Fever	91
Convulsions	14
Altered mental state (irritability apathy lethargy delirium stupor coma)	83
Clear sensorium	3
Signs of meningeal irritation (nuchal rigidity Brudzinski and Kernig signs)	90
Cranial nerve involvement	16
Paresis or paralysis of extremities	3
Sphincteric disturbances	9
Bleeding from ears	9
Bleeding from nose	4
Cerebrospinal fluid rhinorrhea	10
Cerebrospinal fluid otorrhea	[illegible]

of a dural defect in another patient The third patient recovered from the meningitis after the use of sulfonamides but died during operation for the repair of a dural fistula

TABLE 5—*Causative Organisms in Ninety-one Cases of Post-Traumatic Meningitis**

	No of Cases
Pneumococcus	47
Hemolytic streptococcus	11
Streptococcus viridans	2
Streptococcus gamma	1
Hemophilus influenzae	14
Meningococcus	9
Staphylococcus	5
Klebsiella pneumoniae	1
Listeria monocytogenes	1
Total	91

* Data modified from those of Appelbaum and Abler[17]

Postmortem Findings—Autopsies were performed in 11 of the fatal cases, in all of which the presence of purulent meningitis was demonstrated A fractured skull was found in seven of the cases, in four of which the skull roentgenogram was reported as negative for fracture Two of the patients with skull fracture also showed laceration of the brain In one of the patients with fractured skull there were pneumonia and mastoiditis, and in another there was hydrocephalus Two of the patients showed a penetrating injury of the skull and brain There were two instances of frontal lobe abscess, one of which could be definitely traced to an infection of the right frontal sinus and showed in addition a defect in the frontal bone In the other case, the abscess was probably also related to a frontal sinus infection, although this could not be determined with certainty

Comment

It is clear from this study that the head and face injuries involved in post-traumatic meningitis are generally of a severe nature As previously noted, fracture of the skull was demonstrated in 48 instances and presumably was present in many of the remaining cases That skull fractures, associated with dural tears constitute the predominant type of injury in traumatic meningitis has been emphasized by Eagleton,[1] Lewin,[2] Berk,[3] and others Trauma to the frontal area, which contains the nasal sinuses, is particularly hazardous, since the dura in this region can be easily stripped from the bone and result in fistulous communications, allowing the entrance of organisms from the nasal passages As noted by Lewin[2] and Calvert and Cairns,[4] the associated presence of cerebrospinal fluid rhinorrhea renders the meninges even more vulnerable to infection

In the temporal region of the skull, fractures are less likely to lead to separation of the dura and subsequent infection However, a fracture across a chronically infected mastoid, associated with an inflamed dura, may lead to meningitis even in the absence of a dural tear This has been noted in one of the cases in this series It would thus seem that adhesions may, on occasion, serve as a pathway for infection, as suggested by Linnel and Robinson[5] and Hurff and Beling[6]

Fractures through the cribriform plate, where the dura cannot usually be separated from the bone, may lead to meningeal infection if there is a wide defect between fragments or displacement of pieces of bone through the dura In this connection, it is important to stress that complete healing of dural tears is rare More often the fracture line is covered only by a thin layer of fibrous and vascular strands, with the dural tear adherent to the bony margins, or by the sinus mucosa which adheres, as a rule, to the dural edges or to brain tissue This type of repair, as noted by Lewin,[2] constitutes an ineffective barrier against infection, even after a lapse of several years It is also necessary to mention that on a rare occasion a brain abscess which resulted from previous trauma may lead to the development of meningitis as a result of either spontaneous rupture or operative intervention Two cases of this type were encountered in this series At times skull fracture is followed by purulent otitis and mastoiditis or suppurative sinus thrombosis, with subsequent meningeal infection It is probable that the instances of meningitis following the burn on the neck and the dog bite on the face were due to complicating suppurative thrombophlebitis

The occasional occurrence of meningitis following a mild traumatic episode has been recorded by Morley and Hetherington,[7] Norman,[8] Schneider and Thompson,[9] and Beauchamp and Benjamin[10] However, in several of these authors' cases the presence of a dural fistula, cerebrospinal fluid rhinorrhea, or both, were demonstrated, denoting that the head injury in those instances was actually not of a minor character In this connection it is important to bear in mind the limitations of radiology in demonstrating basal fractures of the skull This point is well illustrated by the experience in this series, in which a fractured skull was found

TABLE 6—*Treatment and Outcome in Ninety-one Cases of Post-Traumatic Meningitis*

	Treatment Regimens and Results								
	Before Chemotherapy Antiserum When Available			Sulfonamides Alone			Antibiotics With or Without Sulfonamides		
Etiologic Organism	No of Cases	Recovered	Died	No of Cases	Recovered	Died	No of Cases	Recovered	Died
Pneumococcus	14	0	14	18	5	13	15	14	1
H influenzae	7	2	5	6	3	3	1	1	0
Hemolytic streptococcus	10	1	9	1	1	0			
Nonhemolytic streptococcus	2	2	0	1	1	0			
Meningococcus	7	0	7	2	2	0	3	3	0
Staphylococcus	2	0	2						
K pneumoniae				1	1	0			
L monocytogenes							1	0	1
Totals	42	5	37	29	13	16	20	18	2

at operation or at autopsy in 7 of 16 cases with normal roentgenograms

Considerable attention has been focused on the interval between the trauma and the development of meningitis It may be noted from table 2 that the meningeal infection can occur shortly after the injury, even within a few hours, or years later From reports in the literature and from this studv it appears that the first few weeks after the accident constitute the most dangerous period for the onset of meningitis Of special interest are several reports [11] on the occurrence of meningitis 10 to 16 years after injury

From a clinical point of view, the symptoms of special interest are bleeding from the nose or ears and cerebrospinal fluid rhinorrhea or otorrhea It would seem from this study, however, that these symptoms are not nearly as frequent as is generally expected With few exceptions, the presence of cerebrospinal fluid rhinorrhea is indicative of a fracture involving the frontal, ethmoidal, or sphenoidal sinuses The occurrence of rhinorrhea and otorrhea in only 15 of the patients in this series represents a lower incidence than that noted by other workers As previously mentioned, the flow of cerebrospinal fluid increases the risk of meningeal infection, which may develop shortly after the appearance of the rhinorrhea or otorrhea, or many years later

With respect to bacteriology, it is obvious from table 5 that the pneumococcus predominates as the etiologic agent in this form of meningitis Reports in the literature show a distribution of organisms similar to that noted in this series On rare occasion the meningitis may be caused by more than one organism, by less common bacteria, or the cause may remain undetermined because of a sterile spinal fluid

The striking improvement in the case fatality rate following the introduction of chemical and antibiotic therapy is obvious and points up the urgency of prompt diagnosis It is interesting to note, however, that five recoveries were encountered in the pre-sulfonamide era In these cases, recovery followed the use of specific antiserum in two instances of influenzal meningitis and appeared to be spontaneous in the three patients with streptococcal meningitis The possibility of spontaneous cures in the latter disease has been stressed by Gray,[12] Dandy,[13] myself,[14] and others

It is of interest that such serious residua as deafness, unilateral blindness, and mental impairment were observed in only five of the recovered patients Furthermore, in the mentally retarded case there was evidence of serious brain damage prior to the onset of the meningitis These results are in accord with the relatively low incidence of neurological sequelae among patients recovering from meningitis after the use of sulfonamides or antibiotics

The occasional occurrence of repeated bouts of meningitis following cranial trauma is a disturbing problem As previously noted, each of the three cases of recurrent meningitis in this series was associated with fractured skull and persistent cerebrospinal fluid rhinorrhea Several investigators [15] have stressed that the basic factor in the pathogenesis of rhinorrhea and of recurrent meningeal infections is the presence of bony and dural defects, resulting in a fistulous communication between the subarachnoid space and the nasal cavity While the defects usually are due to trauma, they

TABLE 7 —*Data on Three Patients with Recurrent Meningitis*

						Episodes of Meningitis				
Case No	Age Yr	Sex	Type of Injury	Date of Injury	Rhinorrhea	Dates	Causative Organism	Treatment	Outcome	Remarks
1	24	M	Fractured nose and skull	1937	Persistent	1937			Recovered	
						1939		Sulfonamide	Recovered	
						1941	Pneumococcus type 10 (blood and spinal fluid)	Sulfonamide	Recovered	
						1942	Pneumococcus type 10 (blood and spinal fluid)	Sulfonamide Dural repair	Died	Meningitis cleared died during operation
2	7	F	Fractured skull tured	1939	Persistent	Oct 1941	Meningococcus	Sulfonamide	Recovered	
						Feb 1942	Meningococcus	Sulfonamide	Recovered	
						Nov 1942	Pneumococcus type 33	Sulfonamide	Recovered	On follow up in 1953 patient normal no rhinorrhea
3	12	M	Fractured skull	1951	Persistent	1951 (9 mo after injury)	Pnuemococcus type 18	Penicillin	Recovered	
						Aug 7 1953		Penicillin	Recovered	Operation 1956—fractured ethmoid with projection of dura and brain repair with fascia developed anosmia
						Sept 21 1953		Penicillin sulfonamide	Recovered	
						July 20 1954		Penicillin sulfonamide tetracycline	Recovered	
						Dec 28 1955	Pneumococcus	penicillin sulfonamide	Recovered	On follow up in 1958 patient well no rhinorrhea partial return of sense of smell

may on rare occasion be caused by a tumor or osteomyelitis, as in cases cited by Schroeder [15a] and by Morley and Hetherington [7] The latter authors also mention instances of recurring meningitis associated with rhinorrhea, but without obvious bony defects and dural tears There are reports [16] of recurrent meningitis in the absence of rhinorrhea and also when there is no history of trauma However, in one of these cases without rhinorrhea during life, defects in the cribriform plates were demonstrated at autopsy Similar observations have been made at operation in other instances of recurrent meningitis in the absence of rhinorrhea Schneider and Thompson [9] have also pointed out that cerebrospinal fluid drainage need not occur in the presence of a dural defect, but that protrusion of denuded filaments of the olfactory nerve or extruded brain tissue may serve as a wick along which organisms reach the intracranial cavity

There are some other features of interest in connection with recurrent meningitis As may be noted from table 7 and also from reports in the literature, there may be just two or three recurrent meningeal episodes in a relatively short time, or there may be recurrences scattered over a number of years, with long intervals between the attacks Different organisms are, as a rule, isolated from the spinal fluid during the different episodes On occasion, however, the same organism may be recovered during several attacks The pneumococcus appears to be the most frequent etiologic agent Occasionally no organisms are isolated

The chemical and antibiotic therapy of each recurring meningeal episode is dependent on the etiologic agent In order to stop recurrent or persistent cerebrospinal fluid rhinorrhea and to prevent recurrent bouts of meningitis, it is necessary to close the fistulous dural communication by means of fascia lata transplants It should be noted that in covering the cribriform plates, the olfactory bulbs must be sacrificed, resulting in anosmia However, partial return of the sense of smell may occur at a subsequent date, as was noted in one of the cases in this series

Summary

Ninety-one cases of post-traumatic meningitis were studied Practically all of these occurred after severe trauma to the head or face While definite evidence of a fractured skull was noted in only 48 instances, it is a reasonable assumption that a fracture was present in many of the other cases The interval between the injury and the development of meningitis varied considerably, with a range of from several hours to five years The important symptoms of bleeding from the nose or ears and cerebrospinal fluid rhinorrhea or otorrhea were not nearly as frequent as in generally believed The pneumococcus predominated as the etiologic agent in this form of meningitis As expected, the high case fatality rate in the prechemotherapeutic era contrasted sharply with the striking improvement in mortality following the introduction of sulfonamides and antibiotics

In this series there were three cases of recurrent meningitis Each instance was associated with fractured skull and persistent cerebrospinal fluid rhinorrhea

Foot of East 15th St (9)

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MEPROBAMATE AND SMALL AMOUNTS OF ALCOHOL

EFFECTS ON HUMAN ABILITY, COORDINATION, AND JUDGMENT

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and
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This study was designed to determine whether a combination of meprobamate and alcohol interferes with human ability, coordination, and judgment more than either of these drugs taken singly Eight psychological tests were used to measure the effects of the drugs, which were administered blind to 22 normal subjects Sufficient alcohol was used to produce a concentration of 0 05% in the blood Meprobamate dosage was 400 mg four times daily for a week before the test Four rotated drug conditions were provided (1) placebo tablet and placebo drink, (2) meprobamate tablet and placebo drink, (3) alcohol drink and placebo tablet, and (4) meprobamate tablet and alcohol drink Over all test performance was best in condition (1) and worst in (4) It is recommended that physicians who prescribe meprobamate warn their patients of the increased danger of consuming alcoholic beverages

In view of an earlier investigation by us [1] showing that alcohol has an increased effect on human coordination and judgment when it is combined with chlorpromazine, the question of a possible like effect from alcohol combined with meprobamate arose The question is a practical one because of the large number of persons taking meprobamate who also drink alcoholic beverages, and who may then drive automobiles or operate other dangerous machinery

Kopmann and Hughes [2] found a potentiating effect on test performance of rat subjects when meprobamate was administered with alcohol Marquis and co-workers [3] found no such effect in human subjects However, in the latter study less than 1 oz of alcohol was used, no attempt was made to adjust alcohol consumption to body weight, and the conditions of administration were such as to make the alcohol blood levels at the time of testing highly problematical Moreover the experimental situation was not comparable to the life situation in that meprobamate was administered only at the time of testing A common prescription for meprobamate is 400 mg , to be taken four times daily, and it is in the resultant condition that the user takes an alcoholic drink

Experimental Problem and Procedure

The experimental problem was defined in terms of the null hypothesis there is no more effect on human performance and judgment from a combined dosage of alcohol and meprobamate than from either of these drugs taken singly Twenty-four employees of Madison State Hospital volunteered to act as subjects They ranged in age from 20 to 39 years Twenty-two finished the project, 10 were men and 12 were women They were aware that they would take meprobamate and alcohol but were ignorant of the order of administration

Subjects were randomized into four subgroups of five or six and given a practice session on each of eight psychological tests used Tests were administered under four experimental conditions, (1) placebo (placebo tablet and placebo drink), (2) meprobamate (meprobamate tablet and placebo drink), (3) alcohol (alcohol drink and placebo tablet), and (4) meprobamate plus alcohol (meprobamate tablet and alcohol drink) The four conditions were balanced by rotating them in four different sequences Each subgroup of subjects was assigned a different sequence

Subjects took 400-mg tablets of meprobamate four times daily for a week prior to testing to approximate the usual situation Since placebos were taken in the same manner, a week was provided for the effects of meprobamate to be dissipated before resumption of testing

Sufficient 95% ethyl alcohol was administered to subjects in a lime-lemon carbonated drink to produce an estimated 0 05% blood alcohol level This level is not sufficient to impair automobile driving ability according to a number of United States court decisions Testing of blood alcohol level was by means of a breath analyzer (Breathalyzer) A placebo drink was used on two of the four test days

A battery of eight psychological tests was employed The first test was administered individually and involved matching the lengths of two lines in Muller-Lyer and vertical-horizontal illusions The remaining seven tests were of the paper and pencil

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Consulting Psychologist (Dr Zirkle) Superintendent and Chief Medical Director (Dr McAtee) Clinical Director of Female Service and Director of Clinical Research (Dr King) Madison State Hospital and Sergeant and Director of Charlestown Post Laboratory Indiana State Police (Sgt Van Dyke)

variety and were administered to an entire subgroup The group tests were (1) a mental division test, requiring that three-place numbers be divided by the number seven, time limit, two minutes, (2) a digit-alphabet test, requiring that letters be written below numbers according to a jumbled key, time limit, two minutes, (3) a digit span backward test with number groups from three to nine being given, (4) a test of speed of free word association, beginning with a self-chosen word, time limit, one minute, (5) a test of speed of serial subtraction by the number 3 beginning with the number 100, time limit, one minute, (6) a test of speed of crossing out groups of four dots randomly printed in rows with dot groups of other denominations, time limit, three minutes, and (7) a test of mental addition of 37 to lists of two-place numbers, time limit, two minutes Test administration was in this order The total elapsed time for the eight tests was about 20 minutes

Two of the experimenters made clinical notes on the behavior of subjects during sessions in which alcohol was given At the end of his final test session, each subject was asked to record an evaluation of his relative efficiency and control during the different test sessions, without being told what drug conditions obtained in each

TABLE 1 –*Comparison of Test Results of Twenty-two Subjects Under Four Experimental Conditions**

Test	Placebo		Meprobamate			Alcohol			Meprobamate Alcohol		
	%	Rank	%	Rank	t	%	Rank	t	%	Rank	t
Digit alphabet	27 4	1	25 9	2	2 80*	24 8	3	4 08*	21 9	4	4 30*
Mental division	28 6	1	26 0	2	1 85	24 4	3	3 05*	21 0	4	3 41*
Dots	27 3	1	25 9	2	0 83	24 9	3	2 48*	22 0	4	3 40*
Digit span backward	28 9	1	26 5	2	0 89	24 3	3	1 93	20 3	4	2 75*
Word association	26 5	1	25 7	3	0 83	25 8	2	0 54	22 0	4	2 68*
Mental addition	26 7	1	25 9	2	0 37	25 1	3	1 58	22 3	4	2 33*
Serial subtraction	26 1	2	26 5	1	0 30	24 4	3	1 29	23 1	4	2 07
Illusions	28 3	4	22 7	1	2 55*	24 3	2	2 09*	24 8	3	1 67

* p<0 05

Results

In the alcohol condition, blood alcohol levels ranged from 0 040 to 0 065%, with a mean of 0 049% and a standard deviation of 0 0051 In the meprobamate-alcohol condition, blood alcohol levels ranged from 0 040 to 0 060%, with a mean of 0 051% and a standard deviation of 0 0056 The *t* value of the difference between levels in the two conditions was 1 13, which is not significant

Raw scores for a given test under all four conditions were totaled and the relative percentage of the total for each condition determined These percentages are shown in table 1, along with the relative rank of each (1 being the highest rank), and *t* ratios of the difference between scores in the three drug conditions compared with the placebo condition

With few variations, table 1 shows that performance was best in the placebo condition Progressive deterioration in scoring level occurred from the meprobamate through the alcohol to the meprobamate-alcohol condition, which showed the worst performance The illusions test reversed the trend shown with the other tests, since placebo performance on it was worst In our earlier work with chlorpromazine, the illusions tests appeared to have discriminatory value Its reverse performance in this experiment calls its value in this type of work into question, however If illusions tests results are omitted from calculation, and the placebo percentage of success on the other seven tests is counted as 100%, the comparative percentages of success in the drug conditions are as follows meprobamate 95%, alcohol 90%, and meprobamate-alcohol 80%

Scores in the meprobamate-alcohol condition were significantly lower than those in the placebo condition on six of the tests, with the difference on a seventh just missing significance This contrasts with significantly poorer scores on three tests in the alcohol condition and on only one test in the meprobamate condition These results show that test performance was most adversely affected by the combination of meprobamate and alcohol This is further demonstrated when combined percentages on tests in the drug conditions are compared with placebo percentages (table 2) The greater interference with scoring level in the meprobamate alcohol condition is demonstrated regardless of whether calculations are based on seven or on eight tests When results in the meprobamate-alcohol condition are compared with results under the separate drug conditions, the same pattern of greater interference from the combination of the drugs appears This is shown in table 3

Scores on six tests were significantly worse in the meprobamate-alcohol condition The same was true for the alcohol condition in the case of three tests When performance on all eight tests in the meprobamate-alcohol condition is compared with performance in the meprobamate condition, the *t* value of the difference is significant at the 0 01 level A like comparison with the alcohol condition gives a *t* value which is significant at the 0 01 level Performance in the combined drug condition was therefore significantly worse than in either of the separate drug conditions

Clinical Observations and Self-reports of Subjects.—According to the clinical judgments of two of the experimenters, the combination of alcohol with meprobamate produced more intoxication effects than the alcohol alone in 16 of the 22 cases. On the day of the combined drug dosage, four of the subjects were quite obviously drunk. They showed marked muscular incoordination and little or no concern for the social proprieties. Nothing approaching this was observed in the alcohol condition. One subject cried uncontrollably and afterward was largely amnesic for the period. Two could not walk without assistance.

Self-reports recorded by subjects in response to questions at the end of the experiment fully supported clinical judgments of the experimenters. Seventeen of the 22 subjects said that control of their physical and mental faculties was interfered with most in the meprobamate-alcohol condition. Eighteen judged they would have been most unsafe as drivers in the combined drug condition. Thirteen of 17 subjects who reported a "don't care" attitude during the tests said that it either appeared only in or was greatest in the combined drug condition. Sixteen of 20 subjects who reported sleepiness during the testing sessions said they were sleepiest in the combined drug condition. Subjects generally identified the alcohol condition as being next to the combined drug condition in its interference effects.

TABLE 2.—*Comparison of Placebo Condition with Drug Conditions on All Eight Tests and on Seven Tests (Illusions Omitted)*

	Eight Tests		Seven Tests	
Condition	t	p	t	p
Meprobamate	0.50		3.31	<0.02
Alcohol	1.84	<0.50	4.75	<0.01
Meprobamate alcohol	3.45	<0.02	7.67	<0.001

Comment

Objective test results, clinical judgments of experimenters, and self-evaluations of subjects all indicated that the null hypothesis stated earlier should be rejected. There was more effect on human performance and judgment from a combined dosage of meprobamate and alcohol than from either of these drugs taken singly. The experimenters were frankly not prepared for the extent of the effects. The earlier investigation with chlorpromazine,[1] generally considered a stronger drug, produced much less behavioral deterioration. Results indicate a supplementary and possibly potentiating effect of meprobamate on alcohol. They also indicate that physicians prescribing meprobamate should warn patients of the greater effect from drinking alcoholic beverages while taking the drug—especially if they are likely to operate motor vehicles or other complex machinery.

TABLE 3.—*Meprobamate-Alcohol Condition Compared with Meprobamate and with Alcohol Conditions*

	Condition			
	Meprobamate		Alcohol	
Test	t	p	t	p
Digit alphabet	3.08	<0.01	3.15	<0.01
Mental division	2.78	<0.05	2.12	<0.05
Dots	2.31	<0.05	1.91	<0.10
Digit span backward	4.07	<0.01	1.75	<0.10
Word association	2.52	<0.05	2.85	<0.01
Mental addition	1.85	<0.10	1.79	<0.10
Serial subtraction	2.14	<0.05	0.72	<0.50
Illusions	1.31	<0.50	0.05	
All eight	4.02	<0.01	4.89	<0.01

Conclusions

According to performance on a battery of eight psychological tests, clinical observations by experimenters, and self-evaluations by volunteer subjects, small amounts of alcohol (50 mg %) were shown to significantly impair performance and judgment when combined with meprobamate (400 mg taken four times daily). It is therefore recommended that physicians warn patients taking meprobamate of the potential danger from drinking alcoholic beverages.

The meprobamate tablets used in this study were supplied by Wyeth Laboratories, Philadelphia.

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BRITISH MUSEUM.—In the British Museum there are two copies of Linacre's translation of the fourteen books of Galen's Methodus Medendi. They are in the finest possible condition, and are the presentation copies of Henry the Eighth and Cardinal Wolsey. The title of the King's copy is illuminated with the royal arms, that of Wolsey's is decorated with the Cardinal's hat.—The Gold-Headed Cane, London, J. Murray, 1828.

SPECIAL CONTRIBUTION

CLINICAL RESEARCH FACILITIES GRANTS OF THE NATIONAL INSTITUTES OF HEALTH

G Halsey Hunt, M D
and
G Donald Whedon, M D, Bethesda, Md

The establishment of a program of grants to create specialized facilities in support of clinical investigation of the highest quality has been widely recognized as an important and necessary step in the improvement and intensification of medical research Such a program is being developed by the National Institutes of Health in response to a specific mandate by Congress and a 1960 appropriation of $3,000,000 for this purpose Although the program is in its first stages, it is already evident that it will provide a means not only of enhancing the quality of research applied to patients but also of bringing much more rapidly to those afflicted by disease the accomplishments of sound laboratory research

The prompt response and intense interest of medical centers and institutions with respect to this new program shows that (1) clinical research has hitherto been haltingly and inadequately pursued for a lack of adequate means to provide the careful observation and control needed for research in that complex organism, the human being, and (2) completed, potentially very useful research carried out in animals or in chemical laboratories has, to a significant degree, not been carried over to the logical correlative study of patients because of the absence of the conditions which permit a clear and definite result in the human being The new special grant program will permit competent clinical investigators to overcome these serious deficiencies in the application of research for human benefit

Congressional Recommendation

The Senate Committee on Appropriations expressed in a report[1] its belief that these needs can best be met if special research facilities centers, or units are established in a number of locations throughout the country, providing local sponsoring institutions with a modality for the careful control of clinical studies in any one or more of the many research areas represented by the several institutes It was recognized that one of the principal reasons for the lack of such facilities in academic institutions is the cost of maintaining the highly trained personnel essential to their proper functioning

These recommendations were implemented by the addition of $500,000 to the appropriations for each of six of the National Institutes—those for cancer, mental health, heart, arthritis and metabolic diseases, allergy and infectious diseases, and neurological diseases and blindness—making a total of $3,000,000 The appropriation for the fiscal year 1961, which began on July 1, 1960, is expected to include at least $3,000,000 for this program

Organization of the Program

The director of the NIH, believing that the program would be best administered by a single staff, particularly in its formative years, requested the Division of General Medical Sciences to assume this responsibility and to develop the program with the advice of the National Advisory Health Council At their meetings in November, 1959, the advisory councils of the six institutes involved approved resolutions concurring in the need for central review and advice to the surgeon general on this program and recommending to the surgeon general that he approve applications for clinical research facilities recommended by the National Advisory Health Council The assistant director of the National Institute of Arthritis and Metabolic Diseases, an experienced clinical investigator, was assigned to work part-time with the staff of the Division of General Medical Sciences in developing plans and policies for the establishment of the facilities and in negotiating with and providing advice to interested medical research institutions

The National Advisory Health Council, during its November meeting, conferred with the director of the National Institutes of Health on general plans and policies and agreed to the appointment of a special committee on clinical research facilities This committee consists of six professional members of the council and eight *ad hoc* special advisors These additional consultants bring to the committee representation from other national advisory councils, physicians experienced in research, and a distinguished hospital administrator

Concept

A clinical research facility supported by this program is designed to be a resource within a medi

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Chief, Division of General Medical Sciences (Dr Hunt), and Assistant Director, National Institute of Arthritis and Metabolic Diseases (Dr Whedon), National Institutes of Health Public Health Service, Department of Health, Education, and Welfare

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FOUR QUESTIONS—TWO UNANSWERED

ONE method of assessing end-results in cancer therapy is based on an analysis of the survival rates of the treated patients Individual surgeons or radiotherapists are correct in assuming that the survival rates will afford the answer to the question "How fast does cancer kill my patients?" but because of the many variables involved, the answer must be of a descriptive nature, with care exercised in generalized interpretations of the data We often see reports in which the survival rates observed at various institutions are compared, in an attempt to evaluate the relative efficacy of the program in cancer therapy which each center has adopted Epidemiologists are wary of comparing survival rates in patients attending individual hospitals or clinics Enough assurance must be offered that the many variables inherent in the patient—age, sex, and type and stage of the neoplastic process—have been controlled in all the groups studied, before any valid conclusion may be drawn about the method of therapy

On other occasions, attributing interpretative potentialities to descriptive data results in the extrapolation of site-specific survival rates derived from the experience of a given institution to all patients with homologous malignant neoplasms The epidemiologist believes that variables besides efficacy of treatment preclude attributing to all patients at large the survival rates derived from a single center's isolated experience There is also a tendency among authors to report only those data which are comparable or better than those already existing in the literature As a consequence of eliminating the poorer results, the published reports reflect only the better survival rates on which they are based Furthermore, any analysis of the survival of *treated* patients will necessarily exclude from the computations the survival experience of those individuals who were known to have cancer, but received no treatment for it The exclusion of these patients adds to the limitations inherent in the use of selected material

These considerations form the background of a report on survival in thyroid cancer appearing in this issue of THE JOURNAL, p 1795 Mustacchi and Cutler have included in the study group all the known cases of malignant neoplasms of the thyroid gland which were diagnosed in the entire population of the state of Connecticut during the period 1935-1951 Cases were included solely on the basis of diagnosis, regardless of the modality of treatment employed or whether any therapy had been undertaken

Cancer of the thyroid gland is frequently considered a neoplasm of borderline malignancy, which is certainly at variance with the results of the Connecticut study One-half of all the patients with cancer of the thyroid gland were dead three and a half years after diagnosis As a comparison, it may be noted that the median survival among women who developed breast cancer in Connecticut during the same period of study was somewhat better, just over four years Only in the subgroup of women with the papillary variety of thyroid cancer was the median survival less drastically reduced, but it still fell short of the value of 10 years which was the median survival of the Connecticut women with the relatively slow-growing skin cancers

The impact of cancer of the thyroid on the longevity of the study group can be appreciated even more vividly by pointing out that one-third of the thyroid cancer patients had died within a year of diagnosis, whereas in the absence of thyroid cancer, the same proportion of deaths would have occurred only as late as the end of the 12th year Thus, by studying all the cancer cases diagnosed within a defined population, the epidemiologist may offer an answer to the question "How much does cancer affect the longevity of the community?" This leads to a third question which, as yet unanswerable, may be considered here

We have seen individuals whose residual or recurrent malignant disease, though clinically demonstrable, remained quiescent for some time before becoming biologically active and lethal Moreover, at autopsy, a certain number of individuals, whose death was not related to cancer of the thyroid, disclose the presence in this gland of an occult malignant neoplasm which had remained clinically silent during life The epidemiologist dreams about studying thyroid cancer in a basic population comprising all existing cases, not merely those diagnosed If this improbable situation materialized, epidemiologic studies would probably identify certain parameters characteristic of those individuals who appear to be able to induce dormancy in the thyroid malignancy and those unable to do so Thus, a tentative answer to the third question "What triggers the growth of an occult cancer of the thyroid?" might be reached

Not much is known about the mechanisms of human resistance to cancer However, there is little doubt that, variable as they may be, they exist. We know that our bodies can harbor neoplastic cells and establish with them a temporary symbiosis. Again, one is tempted to consider cancer *in situ,* not only as a histopathologic entity, but also as a statistical concept. In fact, if the pathologist states that a lesion is potentially malignant, it means that sometimes it becomes invasive and sometimes it regresses. What conditions the evolution or the involution of the lesion? We do not know, but, on the basis of the work of Mustacchi and Cutler, epidemiologic evidence suggests that the factors responsible for the development of cancer of the thyroid differ from those that stimulate its subsequent growth.

To the physician interested in prevention (and prevention is the ultimate aim of medicine), this opinion is interesting because it suggests the possibility that two separate control programs might eventually be developed—one to keep an occult thyroid cancer in abeyance and another to prevent its development in a healthy person.

The answer to the final question "Why does thyroid cancer occur?" lies probably in the domain of the biologically oriented laboratory investigator. Still, effective prevention can conceivably be developed even in the absence of this answer by intercepting or manipulating any of the many links in the ecologic chain of events leading to disease. It is in the identification of these links that the epidemiologist meets one of his greatest challenges and can hope to lend some of his most fruitful contributions.

VITAMINS—GOOD OR BAD

The neologopoiesis of the term vitamin—vital amine—in 1912 by Casimir Funk was a milestone in medicine. Food cereal manufacturers, bread makers, soft-drink bottlers, as well as the manufacturing chemists, the pharmaceutical industry, and druggists have exploited to the maximum this vast field of interest. The vitamin content of processed foods has been used and abused as a promotional "gimmick" to such an extent that this, along with over-the counter purchase of vitamins, has pushed vitamin sales figures above the $350,000,000 mark. The physician and his patient at times have appeared to play a secondary role in the drama when, in fact, their interest and financial means should have been paramount at all times. The prevention of a deficiency state or the promotion of maximum well-being through vitamins as naturally occurring constituents of food or supplements in selected clinical conditions needs no comment. But this is not always sufficient, according to the American way of life. If a small quantity of a vital substance is desirable, a large quantity should be highly desirable. In the case of vitamins, supplementary quantities may constitute dissipation and waste in selected few instances, structural harm may result from the superabundance.

It is reassuring to note that the daily requirements of thiamine in an average American diet are met in an adequate fashion, regardless of the quantity of polished rice that is consumed. It would be most unusual to have either a child or an adult develop scurvy with the abundant sources of ascorbic acid in the Americas. The Council on Foods and Nutrition of the A. M. A., supported by a number of studies, has concluded that adequate diets do not need daily supplements of multipurpose vitamins (J. A. M. A. 169:41-45 [Jan. 3] 1959). In spite of these pronouncements, the fallacy seems widely disseminated that every healthy individual must consume multivitamin pills to maintain this status. On the contrary, only in a deficiency state or in an anticipated deficiency state are vitamin supplements necessary. Under such circumstances it is the responsibility of the physician to recommend supplementary vitamins, and the decision regarding dosage and kind of vitamins must reside in the physician and not in the patient or the public press.

When a deficiency is demonstrated for one or more vitamins or the need seems apparent to prevent the development of a deficiency disease, the possibility of management through diet alone should be explored initially by the physician. In indicated instances, single vitamins or multiple vitamins are prescribed as supplements to the diet. If single or multiple vitamins are ingested, without sound clinical indications, trouble may appear, such as hypervitaminosis A or D. At other times a disease may develop, with the masking of characteristic symptoms. The body is able to tolerate many times the daily requirements of vitamin A, intemperate amounts, however, may lead to anorexia, irritability, cutaneous eruptions, or hepatomegaly. Excessive quantities of vitamin D may lead to gastrointestinal symptoms and later metastatic calcification. If the kidney is the site of calcinosis, renal insufficiency may develop. In recent months our attention has been focused upon the potential harm from indiscriminate ingestion of small amounts of folic acid, usually one constituent of a multiple-vitamin preparation. The Council on Foods and Nutrition and the Food and Drug Administration have been concerned over the possibility of central nervous system deterioration in patients with incipient pernicious anemia, who assimilate modest quantities of supplementary folic acid, with or without specific knowledge of potential harm. Pernicious anemia is not a rare malady. But the insidious nature of its symptoms may escape suspicion if the oral intake of small quantities of folic acid is sufficient to correct the hematologic dysfunction, nervous system changes meanwhile may continue to progress (J. A. M. A. 173:240-244 [May 21] 1960). The value of 400 mcg. (0.4 mg.) per day appears to be a safe figure. No evidence is available indicating that patients with pernicious anemia in relapse will respond hematologically to this quantity of folic acid ingested, in addition to the amount absorbed from an average diet in America

After consultation with a group of qualified hematologists in the United States, the Commissioner of Foods and Drugs has decreed that

Vitamin preparations containing more than 0 4 milligram or 400 micrograms per daily dose be sold only on prescription

For those vitamin preparations containing more than 0 4 milligram (or 400 micrograms) of folic acid, the proposed regulation provides that

1 At the point of manufacture of labeling, the change to prescription labeling be accomplished before further shipment of such products

2 That the orderly relabeling of stocks of such products already in the channels of distribution proceed as promptly as possible

3 That product not properly relabeled after a reasonable period of time be subject to regulatory action

If interested parties do not submit acceptable evidence of the safety of folic acid in amounts up to 0 4 mg per day after March 6, 1961, all preparations containing folic acid would be permitted on a prescription basis only

SINGLE MAMMALIAN CELLS

Recently, techniques were developed to enable an inoculum of single mammalian cells to be quantitatively placed in Petri dishes with a nutrient medium, so that each individual cell multiplies to form a discrete colony This plating procedure made possible rapid and precise titration of the number of cells in any population capable of unlimited multiplication, in a manner analogous to that employed in quantitative bacteriology The same technique was successfully applied to human cells originating in normal instead of malignant tissues

By control of the physical and chemical environment of normal cells so as to minimize toxic or growth-inhibitory conditions, two separate goals were simultaneously achieved Single, normal cells could be plated that they might grow into discrete, isolated colonies, and such cells could be maintained indefinitely in active growth in vitro, without any recognizable deviation from the original chromosomal constitution Thus, two of the most fundamental requirements for cellular genetic studies became available for normal as well as malignant cells Dr Theodore T Puck, Department of Biophysics, Florence R Sabin Laboratories, University of Colorado Medical Center, Denver, emphasizes that certain physical parameters were found to require most careful regulation in order to achieve reliable results in growing normal, diploid mammalian cells

These parameters are temperature, carbon dioxide concentration, maintenance of pH in the region of 7 0 to 7 4, relative humidity, and use of media which are sufficient nutritionally and are free from toxic substances

The nutritional requirements of at least one cell type, the S3 HeLa clonal stock, have been defined and a medium consisting of two purified protein fractions (fetuin and albumin) and a completely synthetic micromolecular complement has been developed which reliably promotes growth of single cells into colonies of any desired size This medium has been found to be far more reproducible in its action than any medium based on whole serum or its dialyzed macromolecular portion Growth is achieved when additional serum fractions are added A high efficiency of single-cell plating and a means of keeping such euploid cells in cultivation at a rapid growth rate for indefinite periods have been achieved by the use of two combined measures substitution of fetal for adult mammalian serum as a growth supplement, and testing of each batch of such serum by the single-cell plating technique, selecting for use only those lots which provide high plating efficiency

Another condition necessary is a periodic recloning by means of which it is possible to return a mutant to a form with chromosomal constitution and biochemical behavior indistinguishable from that of the original culture

A method was developed which would permit establishment of cells in culture from any individual A tiny sample of skin was used, and, by this method, cell cultures could be obtained from large numbers of human subjects Thus, large scale tests on human populations became possible, and cells from humans with known genetic defects could be established in culture and could be used to provide specific markers for genetic studies in vitro

These studies, according to Puck and his coworkers, established that the chromosomes of cells from normal human subjects were remarkably constant in number and morphology, regardless of the age of the person from whom the biopsy was taken or the organ sampled, these included skin, endometrium and myometrium, cervix, bone marrow, testis, ovary, and lung These studies revealed a chromosome number of exactly 46 (or 92 in a polyploid cell) to be displayed by more than 99 9% of cells examined This result established beyond question the original finding of Tjio and Levan that the normal human chromosome number is 46, rather than 48, and made possible experimentation on chromosomal aberrations of humans with genetic defects On the basis of these studies, it proved possible to identify each of the human chromosomes and to assign identifying numbers so that all the individual chromosomes can now be recognized Similar results have been independently obtained for some of the human chromosomes by English investigators and for the entire human karyotype by Chu and Giles

Finally, the chromosomal constitutions of a num ber of genetically aberrant human constitutions have now been defined Thus, French and English workers demonstrated the presence of an extra chromosome of group VIII in patients with Mongolism and the presence of two X chromosomes and a Y chromosome in Klinefelter's syndrome The English investigators and Puck's laboratory demonstrated the absence of one sex chromosome in human gonadal dysgenesis (Turner's syndrome), a disease which displays a total chromosome number of 45 and only a single sex chromosome, the X This study also demonstrated that, in man, the Y chromosome contains the genes for maleness In a female patient suffering from primary amenorrhea, Puck and his co-workers found that the number of chromosomes was 46, but the pattern was that of a male since an X and Y chromosome were present In this case, the defect showed the hereditary pattern of a sex-linked recessive gene, which presumably can prevent normal male expression In a patient with Treacher-Collins disease, the chromosomes were normal in number but possessed marked abnormalities in structure

These examples serve to illustrate some of the new fields of investigation in human biology The gene-enzyme relationships in man will become definitely established in many hundreds of cases New insights into human developmental processes and into the nature of malignancy and aging will result from the combined use of in vitro studies and in vitro techniques under carefully controlled conditions in study of the genetic-metabolic relationships of the human somatic cell

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[1] Puck T T Single Mammalian Cells in Centennial Lectures Commemorating the One Hundredth Anniversary of E R Squibb & Sons New York G P Putnam s Sons, 1959

AORTIC EMBOLECTOMY

Embolus to the aortic bifurcation is a surgical emergency If the obstruction is complete, only by operation within a few hours can one hope to save the life of the patient Without surgical intervention the immediate mortality is at least 75% The prognosis in the patient with a saddle embolus is uncertain, even with successful removal of the clot, because it depends largely upon the disease which is primarily responsible for the embolus Even most poor-risk patients do not die from the operation of embolectomy, most die of gangrene, heart disease, or as a result of amputation

The major etiologic factors for such an embolus are rheumatic valvular heart disease and myocardial infarction with mural thrombi Thrombi in the heart are apt to be dislodged during periods of atrial fibrillation, and the patient suddenly experiences pain, paresthesia, paresis, pallor, and pulselessness of both lower extremities Generally the diagnosis is not difficult (This issue, p 1835)

After the diagnosis has been made the patient should be promptly hospitalized and prepared for embolectomy Evaluation and rapid stabilization of the patient's cardiovascular status by the internist is an essential part of the preoperative preparation The key to success is the performance of embolectomy before thrombosis has occurred distal to the site of the embolus In general, the good results are directly related to the shortness of the interval between the onset of symptoms and embolectomy Most successful embolectomies are performed within six hours after occlusion Technically, the successful removal of an aortic embolus is not difficult, and delicate vascular instruments are not necessary Therefore, every patient with a saddle embolus need not be sent to a cardiovascular center because any full-time surgeon should be competent to perform this operation successfully

Spinal anesthesia offers good relaxation and allows the intestines to be packed out of the operative field more easily The transabdominal approach for exposure of the bifurcation of the aorta and its branches is preferable in that it is rapid and direct A long, midline incision through the transabdominal approach provides this needed exposure of the terminal aorta and the iliac arteries After the posterior peritoneum has been opened and the periaortic tissue has been separated, the common iliac arteries are occluded well distal to the aortic bifurcation to prevent distal migration of the embolus, which might necessitate a further incision If vascular clamps are available, their use at this time is not likely to fragment the distal end of a long slender iliac extension of the aortic embolus, and allow it to propagate distally This could happen, however, and the groins and thighs should be included in the preparation and draping, so that the femoral arteries can be quickly exposed for the extraction of any fragmented clots Occlusion of the aorta proximally may be accomplished simply with an assistant s finger, a hemostatic Rummel-type tourniquet, or preferably with one of the many types of available vascular clamps A 0 1% solution of heparin is injected into the aorta and iliac arteries proximally and distally to the hemostatic occlusions The embolus is evacuated through a vertical anterior aortotomy incision, and the artery is flushed proximally and distally to remove any clot segments Good return flow upon release of the occlusive tapes from the iliac arteries demonstrates the patency of the vascular channels distally, which is a good prognostic sign But, if back bleeding is poor after removal of the main thrombus, firm catheters should be in readiness to extract an additional slender thrombus from the femoral or popliteal arteries, which have already been draped into the operative field Closure of the aortotomy incision can be accomplished accurately and expeditiously with a simple over and over 0000 arterial silk suture Heparin solution is injected into the distal aorta after release of the occlusive tapes The posterior peritoneum is carefully approximated before closing the incision Most patients are given anticoagulants in the postoperative period The prognosis, with respect to the comfort and use of the extremities, will of course depend upon the circulation, which, in turn, depends upon whether the clot has been completely removed

Some physicians believe that aortic embolism carries such a high mortality rate, however treated, that a fatalistic attitude is at times adopted With improved preoperative medical management of cardiac patients, greatly improved anesthetic techniques, monitoring of the heart during surgery, the widespread improvement of vascular surgery in general, and the prevention of further emboli by cardiac surgery, the patient sustaining aortic embolism has a better outlook than he did a decade ago

PHILADELPHIA–ALBUQUERQUE–CHICAGO

Another name has been added to the masthead of The Journal Another position of major responsibility has been incorporated in the structure of the Editorial Division Dr Burgess Lee Gordon became a full-time member of our staff a fortnight ago when he assumed the duties and anticipated the privileges of Associate Editor of The Journal One of his last educational assignments, before moving to Chicago, was the detailed supervision of a treatise entitled "Clinical Cardiopulmonary Physiology," sponsored by the American College of Chest Physicians This is but one of many editorial assignments that reflect credit upon his talents in this field of medicine Since the completion of his formal medical training in the early 1920's, Burgess has served as Associate Editor of the Oxford System of Medicine and as a member of the Editorial Board of *Roentgenology of the Chest* It was clear to those of us who were interested in inducing him to join the editorial staff that his experiences in medical writing and medical journalism were rich and abundant In the program begun several months ago, designed to implement the editorial staff of the scientific publications of the American Medical Association, it was discovered at any early stage that there exists a critical shortage of physicians with capacity and experience in this discipline We were indeed fortunate then to have him look with favor upon our invitation when it was extended early this year

Burgess was born in the Pacific Northwest, in Spokane, Washington The Atlantic Seaboard has claimed him since college days Most of his medical training and professional activities have been pursued in and about Philadelphia He graduated from Jefferson Medical College, interned in Philadelphia, and was attracted to the Peter Bent Brigham Hospital in Boston for a residency in medicine Henry A Christian and Harvey Cushing were the Chiefs of Medicine and Surgery at The Brigham in those days, a brilliant era for The Brigham Burgess returned to his alma mater in Philadelphia, and subsequently was appointed Clinical Professor of Medicine at Jefferson for four years He was President of Women's Medical College and Mullen Professor of Medicine from 1951 to 1957

The triad of medical writing, medical teaching and medical practice, evidence of a full professional life, cannot be broken down into its components in analyzing the accomplishments of Burgess The triad is not divisible His experiences as a clinician, his interests in progress, an indispensable trait for teachers, and his capacity for composition, will be exploited maximally in this new assignment with the American Medical Association A portion of each day will be devoted to inescapable routine activity that each individual must pursue, whether practicing medicine or participating as a member of a medical organization, large or small The successful completion of routine chores is a signal to spend the remaining time cogitating over the past, reviewing the present, or planning for the future In this latter category Burgess is already deeply involved in exploring the possibilities of electronic computers and other incomprehensible mechanical devices as they may be applied to medicine in the immediate or distant future Classification and nomenclature of disease, tabulation, storage, and rapid retrieval of many types of medical data, and abstraction of current literature are three examples that lend themselves to these fabulous machines, eager to solve difficult problems These are items that demand immediate attention, many others will be considered as time goes by The possibilities for maximum utilization of electronic devices in medicine cannot be foretold I believe that the number is legion It is trite, but nevertheless true, that this is an exciting time in medicine

During the many years that our new Associate Editor was claimed by Philadelphia, Doctor and Mrs Gordon resided in Rittenhouse Square, the center of the city Three years ago they moved to Albuquerque where Burgess was Director of Education at the Lovelace Foundation, established by W Randolph Lovelace II and his uncle, W R Lovelace, and the late E T Lassetter at the end of World War II I suspect that this call to Albuquerque was related to mutual interests of our new staff member and Randy Lovelace, when each was serving his country with the armed forces The desert sun and the refreshing way of life were different, delightful, and rewarding in Albuquerque But now the Gordons have returned to city living on the twenty-sixth floor of an ultra modern blue and white apartment overlooking the skyscrapers of the Loop and the blue waters of Lake Michigan

J H T

CLINICAL NOTES

REPEATED SUCCESSFUL AORTIC EMBOLECTOMY

Herbert E Gude, M D, Don C Fields, M D
and
Robert C McAdams, M D, Lafayette, Ind

Without surgical intervention the catastrophe of aortic bifurcation or saddle embolus results in an immediate mortality of 75%, but surgical removal of the embolus within 6 to 10 hours will usually restore the arterial flow Embolism implies serious systemic disease Although most patients survive aortic embolectomy, few of them are alive after five years They die subsequently from further embolic episodes or from cardiac failure

Previous Reports

Bauer performed the first successful aortic embolectomy in 1913 In 1943, McClure and Harkins,[1] in a review of the literature, reported that 21 aortic emboli had been successfully removed Thiessen and Marxen,[2] in 1952, reported that 34 successful aortic embolectomies had been performed, and by 1958 Dale and Mahoney[3] had counted 64 successful embolectomies at the bifurcation Since 1958 six more reports of this operation have appeared in the literature With the advancements in arterial surgery, it is probable that more than the 70 successful operations have been performed but have not been reported Repeated successful aortic embolectomies are rare Nystrom[4] and Westerborn[5] operated separately on the same patient within a two year period The patient survived each aortic embolectomy and lived for five years In 1957, Thomas[6] reported the second repeated successful saddle embolectomy Dale and Mahoney[3] successfully removed three separate aortic emboli within an 11-month period from the same patient In 1959 Hurwitt and co-authors[7] reported a case in which a second aortic embolectomy was preceded by an emergency mitral valvular commissurotomy This is the fifth report of a successful repeated aortic embolectomy

Report of a Case

A 64-year-old housewife was admitted to St Elizabeth Hospital June 16, 1959, due to the sudden onset of pain in both lower extremities The pain lasted for one hour, and then there was numbness, pallor of the skin, and weakness of the lower extremities For 20 years she was known to have had atrial fibrillation She had had congestive heart failure due to rheumatic heart disease about 10 times Thirty years previously a thyroidectomy had been performed for toxic goiter Digitoxin, 0 1 mg daily, had been the only regular medicament taken prior to this hospital admission

Examination of the abdomen gave negative results Both lower extremities were cold and cyanotic No dorsalis pedis, posterior tibial, or popliteal or femoral pulse could be elicited on either side The blood pressure was 160/80 mm Hg The heart rate was 90 beats per minute, and rhythm was irregular The left heart border was percussed to the left anterior axillary line A precordial thrill was present Systolic and diastolic loud apical murmurs could be heard Dry crackling rales could be heard in both posterior pulmonary bases

Laboratory studies revealed the following information hematocrit value, 43 5 vol %, white blood cell count, 7,200 per cubic millimeter, and hemoglobin level, 14 1 Gm % The differential blood count was normal, and urinalysis gave negative results Electrocardiographic report revealed atrial fibrillation and occasional premature ventricular beats

Diagnosis of saddle embolus of the aorta was made, and the patient was taken to surgery and prepared for embolectomy three and one-half hours after the onset of symptoms The operation was performed with the patient under spinal anesthesia A long midline incision was made from the symphysis pubis curving around the umbilicus to within 5 cm of the xiphoid process The general abdominal exploration revealed no evidence of visceral disease The transverse colon and small intestine were brought out onto the abdomen and held in place with moist towels Good exposure of the aorta revealed a strong pulsation to within 3 cm of the bifurcation where the pulses abruptly stopped and where a mass could be palpated within the aorta

The iliac arteries were occluded by DeBakey vascular bulldog clamps, and 5 cc of 0 01% heparin solution was injected into the iliac arteries distal to the vascular clamps The aorta was occluded 7 cm proximal to the bifurcation with a DeBakey aortic clamp, and 5 cc of heparin solution was injected proximally into the aortic lumen A 2-cm longitudinal incision was made on the ante-

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From the Department of Surgery St Elizabeth Hospital rior aorta just proximal to the bifurcation, and an organized clot was removed in one segment This embolus had the configuration of the aorta with two short iliac extensions The iliac vessels were allowed to bleed, and a good flow was obtained Several small clots were flushed out when the proximal aortic clamp was temporarily released The aortotomy incision was closed with a running over-and-over 0000 arterial silk suture The wound was closed with chromic catgut on the posterior and anterior peritoneum, and silk was used for the fascia and skin Femoral pulsations could be palpated before the abdomen was closed because the region of the common femoral arteries had been prepared and draped into the field

At the close of the operation, which lasted one and one-half hours, both lower extremities were warm and pedal pulsations could be elicited, but the feet were cool to the touch No anticoagulants were given in the immediate postoperative period, and no attempt was made to convert the atrial fibrillation to a regular rhythm The patient's course after surgery was uneventful until the fourth day, June 21, 1959, at 8 00 p m At this time she complained of numbness in her right lower extremity Fifteen minutes later she experienced pain in the left inferior extremity On physical examination the five "P's" of aortic embolus were present—pain, pulselessness, pallor, paresthesia, and paresis The patient was again taken to surgery, and a spinal anesthetic was given The previous incision was reopened after the sutures had been removed Again at the bifurcation of the aorta proximally there was a strong pulsation No pulsation was noted in the iliac vessels There was a mass palpable within the aorta Clamps were applied, heparin solution was injected as in the previous operative procedure The sutures were removed from the anterior aortotomy incision, and another organized clot of similar size and configuration was removed Closure of the aortotomy incision was again completed with 0000 running silk Pulsations, color, and temperature returned in both lower extremities

The patient received an initial anticoagulant dosage of 150 mg of phenindione (Hedulin) on morning of second embolic episode Successive daily prothrombin time determinations adjusted the daily dosage after the second embolectomy The postoperative course was uneventful, and on the 14th postoperative day she was discharged

At home she has taken digitoxin, 0 1 mg daily, and the daily dosage of phenindione has been adjusted according to the prothrombin time determination On observation at intervals since her dismissal from the hospital eight months prior to this writing, the patient has had some complaints of low back pain, but the blood supply to both lower extremities has shown no significant impairment She had at the time of this writing palpable pedal pulses, her heart remained in atrial fibrillation, and diuretics have been given on two occasions for basilar lung congestion

Comment

The majority of patients who have an aortic embolus have a significant cardiac history The embolus may have a rare origin like myocardial trichinosis or syphilitic aortitis, but the most common cause of a saddle embolus is a thrombus which has formed in the auricle of a fibrillating heart Frequently a thrombus forms in the wall of the left ventricle after a myocardial infarction, and subsequently it is thrown into the systemic circulation Of all peripheral emboli, obstruction at the aortic bifurcation is one of the most serious, but fortunately it is not common Saddle embolus comprises about 5 to 10% of all peripheral emboli

As a rule, diagnosis is not difficult because of the spectacular signs after sudden aortic occlusion The five "P's" of embolic obstruction are present Pain in the back and both lower extremities usually is the presenting symptom Paresthesia develops shortly, and within hours paresis or paralysis develops in both lower limbs Early examination shows pulselessness of both femoral arteries and their distal branches Pallor is present, and mottling of the skin of both limbs with a decrease in skin temperature occurs afterwards

The treatment of an aortic bifurcation embolus is early embolectomy, although Walker[8] and Albright[9] have reported survivals without operation The time interval between onset of the embolus and surgery is important Most successful embolectomies are performed within six hours after the onset of symptoms Few patients have had the circulation restored after this time because of the formation of extensive small clots below the embolus, which cannot be completely removed

Removal of an aortic embolus is not difficult from a technical standpoint, but a few notes on technique may be worthy of mention The region of the common femoral arteries should be prepared and draped into the field This draping allows for the removal of concomitant or subsequent femoral emboli immediately Return of the femoral pulsations after removal of the embolus may be easily detected before the abdominal wound is closed

A long abdominal incision in the midline is desirable because it gives satisfactory exposure and it can be made expeditiously This long incision allows for easy retraction of the abdominal viscera out of the operative field onto the abdomen This direct transabdominal approach gives excellent exposure to the bifurcation and less handling of the vessels is necessary The retroperitoneal approach, we feel, necessitates excessive handling of the aorta and iliac vessels, and this may propagate the em bolus distally Prevention of this may be accomplished by freeing and clamping the common iliac arteries before the aorta is mobilized once the bifurcation embolus has been palpated

There are several methods described for the occlusion of the aorta and iliac arteries Digital pressure, various tourniquet clamps, and twisted tapes are used according to the preference of the surgeon The DeBakey aortic clamp is the instrument of our choice for occlusion of the aorta proximally, and DeBakey bulldog clamps occlude the iliac arteries efficiently and atraumatically In our experience, problems of fracturing arteriosclerotic vessels have been nonexistent with these clamps The DeBakey aortic aneurysm clamp is used to occlude the lumbar arteries to insure good bloodless visualization of the bifurcation lumen

A longitudinal aortotomy incision over the clot anteriorly is preferred to the iliac aortotomy because with occlusion of all pathways to the distal aorta the lumen can be inspected thoroughly We now feel that a transverse aortic incision is preferable because the closure tends to lessen the narrowing of the aortic lumen Loosening the vascular clamps successively will flush out all remaining clots and will insure the patency of the distal arterial system When there is obstruction in the distal arterial tree, easy access to the femoral arteries is accomplished with proper draping of these areas into the operative field

Recently we have routinely used retention sutures with the long midline incision This omits the possible addition of a wound disruption to an already seriously ill patient Spinal anesthesia has been used because of the following advantages The abdominal musculature is maximally relaxed, and the peripheral vasomotor tone has been abolished This would not be the anesthetic of choice in recent myocardial infarction because of the danger of hypotension

Lumbar sympathectomy after embolectomy probably is not indicated with return of good arterial circulation in the lower extremities, but it may be useful where there is a question of arterial insufficiency It is doubtful, however, that lumbar sympathectomy will save a limb if the embolectomy does not adequately clear the vessels

Routine anticoagulant therapy postoperatively can be contested Madden[10] has reported the largest series of saddle embolectomies of any author, and he has discontinued postoperative anticoagulant usage because of hemorrhagic complications Moore[11] and others agree that embolization is rarely encountered beyond the early postoperative period and that long-term use of anticoagulants to diminish the likelihood of embolization does not seem indicated On the other hand, Proffitt[12] cites an instance when a patient had been on anticoagulants for 28 days and there were no arterial emboli, although one did occur two and one-half days after cessation of this therapy It seems reasonable to visualize a firm thrombotic plaque on the wall of the heart having just released a single thrombus into the systemic circulation, and proper anticoagulant levels would indefinitely prevent further thrombus formation The use of indefinite long-term postoperative anticoagulant therapy probably is in order for chronic fibrillators who are not, for one reason or another, candidates for excision of the auricular appendage or mitral commissurotomy

The management of a patient sustaining an aortic embolus includes embolectomy for the immediate problem and subsequent therapeutic measures to prevent a recurrence of another embolic episode

Summary

The fifth case of repeated successful aortic embolectomy has been reported At the time of this writing the patient is still alive Every victim of aortic embolism should be given the benefit of surgical treatment since operative intervention is the main chance for survival Long-term anticoagulant therapy is useful in preventing further emboli if the patient is not presented for cardiac surgery

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MYOCARDIAL INFARCTION

REPORT OF A CASE IN A SEVENTEEN-YEAR-OLD MAN WHO SURVIVED

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A 17-year-old man presented himself at the emergency room of Cape Fear Valley Hospital on the evening of Sept 20, 1959, complaining chiefly of severe chest pain of one and one-half hours duration The patient was in good health until the night prior to admission to the hospital, when he had an episode of transient nausea and vomiting unaccompanied by pain On the day of admission, about 30 minutes after eating a large evening meal the patient began having severe substernal chest pain which did not radiate He became nauseated and vomited once on the way to the hospital The chest pain continued for one and one-half hours, until the patient was seen at Cape Fear Valley Hospital At that time he complained of numbness in his arms There was no radiation of the pain into the jaw, the arms, or the back

The patient s father, who was 50 years old, has hypertensive heart disease There was no other pertinent family history The patient's own history showed that his general health had been good He had been treated for a "virus infection" in his chest in the spring of 1959 but otherwise had been in excellent health He was a junior in high school and had been attending school regularly

In the emergency room the findings were as follows temperature 98 6 F (37 0 C), pulse rate 80 per minute, respirations 20 per minute, and blood pressure 130/90 mm Hg The patient was thin and was somewhat sullen in his attitude but cooperative otherwise The patient did not appear older than his stated age of 17 He complained of chest pain at the time of the examination but stated that the pain had diminished in intensity since his arrival at the hospital There was severe acne of the face and shoulders The fundi showed normal-appearing arterioles, and there were no hemorrhages or exudates The thyroid gland was not enlarged, the neck veins were not distended, and the lungs were clear except for a few coarse ronchi heard at both bases The heart was not enlarged to percussion, and the rhythm was regular except for rare premature ventricular beats The heart sounds were of fair quality No murmurs or pericardial rubs were heard The abdomen was flat and not tender The liver and spleen were not felt The examination of the extremities showed no edema, and the peripheral vessels and arterial pulsations were entirely normal

A chest x-ray made on the night of admission to the hospital revealed no pathological findings There was no evidence of pneumothorax, and the heart appeared entirely normal in size, shape, and position

On admission to the hospital the patient was given prochlorperazine (Compazine), 10 mg intramuscularly, and was kept in bed The patient s pain subsided completely, and he had no further nausea and vomiting

On the morning after admission to the hospital, Sept 21, 1959, the patient's temperature was normal He stated that he felt fine His heart sounds were of fair quality, and no friction rubs were heard On this date the following laboratory data were obtained Urinalysis showed a specific gravity of 1 012 and contained no albumin or sugar The microscopic examination of the urinary sediment showed 10 to 15 white blood cells per high power field Examination of the blood showed hemoglobin level, 14 2 Gm, hematocrit reading 45 vol %, white blood cell count, 18,000 per cubic millimeter, neutrophil level, 77%, lymphocyte level, 22%, and monocyte level, 1% Serum amylase level was normal An electrocardiogram showed a rate of 70 beats per minute, P-R interval 0 16 seconds, and QRS interval 0 08 seconds There was normal sinus rhythm with occasional premature ventricular beats The electrocardiogram showed changes consistent with an early anterior myocardial infarction Serial electrocardiograms taken during the next few days showed further changes characteristic of anterior myocardial infarction (fig 1 and 2)

On Sept 22 1959, the second hospital day, blood counts showed hematocrit reading of 48 vol% sedimentation rate of 24 mm per hour, and white blood cell count of 16,350 per cubic millimeter Serum transaminase level on the second hospital day was 30 units Fasting blood sugar level was 105 mg % and serum cholesterol level 155 mg % On the third hospital day, serum transaminase level was 45 units A serologic test for syphilis showed negative findings

The patient's course in the hospital was essentially uncomplicated He had no further chest pain after the first night in the hospital and did not require any opiates for relief of his chest pain From the second to the fifth hospital day the patient ran a low-grade fever, but at no time did his temperature go higher than 99 6 F (37 6 C) The patient remained quite comfortable, and at no time was he dyspneic While in the hospital

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From the Department of Medicine Cape Fear Valley Hospital the patient developed a very soft grade 1 systolic murmur heard at the apex and also at the base of the heart He had occasional premature ventricular beats which disappeared after the first week of hospitalization After the diagnosis of myocardial infarction was established, the patient was treated with anticoagulants and was maintained on anticoagulant therapy for the duration of his hospital stay

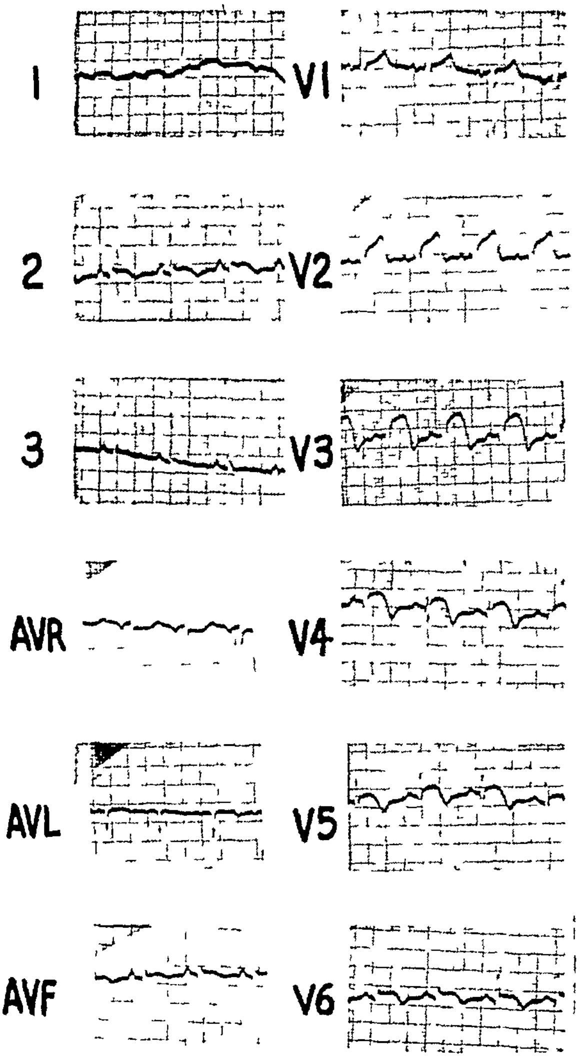

Fig 1 —Electrocardiogram taken Sept 22, 1959, 36 hours after patient's admission to hospital Note early changes of anterior myocardial infarction

For a period of four weeks he was kept at bed rest and then was allowed to sit up Prior to discharge from the hospital the patient was permitted to walk During the last week of hospitalization a routine stool examination revealed the presence of hookworm eggs, and blood cell counts showed an eosinophil level of 7% Treatment of the patient's hookworm disease was deferred until a later date The patient was feeling quite comfortable when discharged from the hospital, on Oct 23, 1959 The final diagnosis was coronary thrombosis with anterior myocardial infarction, arteriosclerotic heart disease, hookworm infection, and acne vulgaris

Since leaving the hospital the patient has been seen on four office visits An electrocardiogram made on Nov 3, 1959, showed the typical inversion and coving of the T waves across the entire precordium (fig 3) Another follow-up electrocardiogram on Dec 1, 1959, showed some improvement in the T wave inversion (fig 4) The patient has had no symptoms of coronary disease since leaving the hospital The hookworm infection was successfully treated in November, 1959

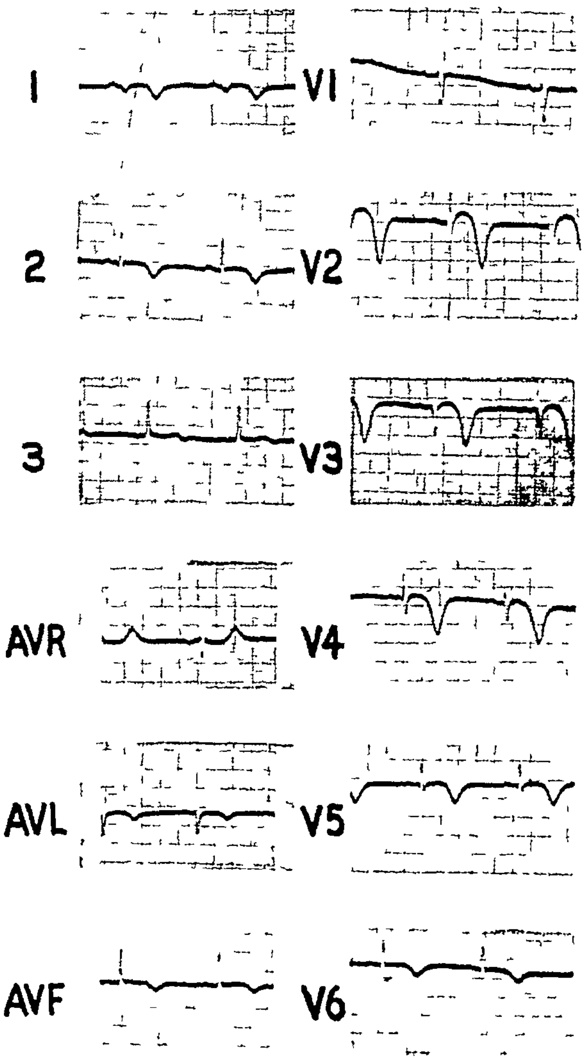

Fig 2 —Electrocardiogram taken Oct 6, 1959 Note deep T-wave inversion and coving across entire precordium

Comment

There have been reports of cases of coronary thrombosis in childhood and in young adult life but so far a search of the literature has not revealed a proved case of myocardial infarction which did not result in death in a patient as young as this Talbot and others[1] in 1945 described a 7½-year-old boy with progeria who had died of coronary occlusion In 1949 MacDougall[2] reported a fatal coronary occlusion in a 16-year-old girl Shivelhood[3] in 1948 described a fatal case of myocardial infarction in a 12-year-old boy with diabetes In a very extensive study, in 1948, Yater and others[4] reviewed 866 cases of coronary artery disease appearing in soldiers aged 18 to 39 years In their series the youngest survivor was 20 years old There was one fatal case of coronary artery disease in a patient aged 18 years in this group

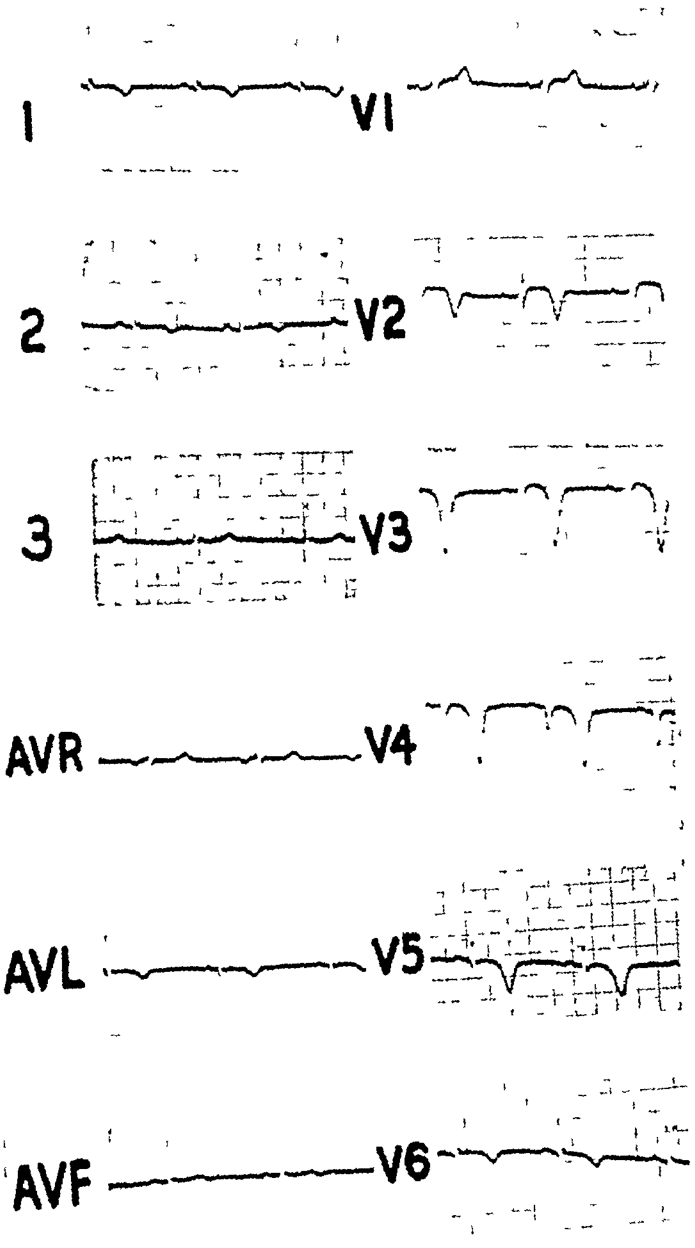

Fig 3—Electrocardiogram taken in office on Nov 3, 1959

Sprague and Orgain[5] reported a case of a 15-year-old boy who had had symptoms of dyspnea and substernal choking on exertion for three years At autopsy the patient was found to have moderate atherosclerosis of his coronary arteries The left circumflex branch was completely occluded by a gray thrombosis The terminal portion of the right coronary artery also had a similar clot

Dr Walter A Stryker[6] wrote a paper entitled "Coronary Occlusive Disease in Infants and in Children" which appeared in the *American Journal of Diseases of Children* in 1946 In this article Dr Stryker discussed eight different causes of coronary occlusive disease in infants and in children and listed examples and cases to illustrate each group Dr Stryker's classification was as follows (1) medial calcification with fibroblastic proliferation of the intima, (2) polyarteritis (periarteritis) nodosa, (3) arteriosclerosis, (4) syphilitic arteritis, (5) embolism, (6) congenital abnormalities, (7) rheumatic arteritis, and (8) hypertension In Dr Stryker's article there were no reports of patients who had coronary thrombosis with myocardial infarction who survived

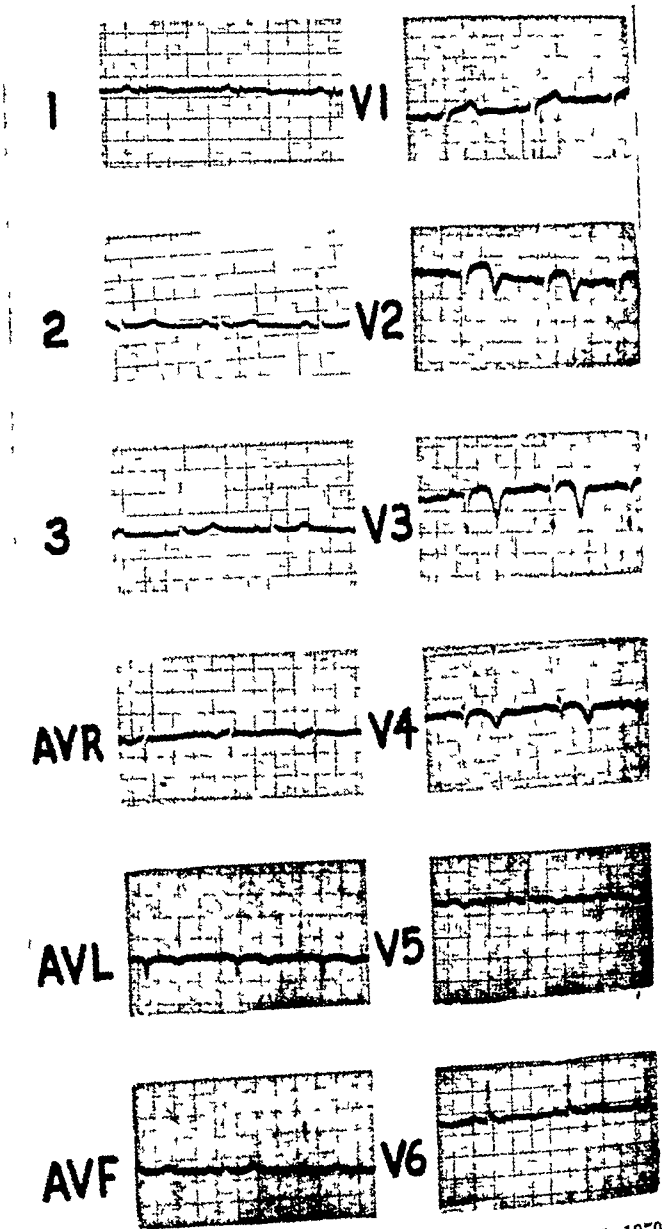

Fig 4—Electrocardiogram taken in office on Dec 1, 1959 Note improvement in T-wave inversion

Summary

A typical myocardial infarction occurred in a 17-year old man In view of the lack of any evidence of complicating or predisposing factors, it is believed that this patient's underlying disease probably was coronary atherosclerosis A review of the literature has not revealed an occurrence of a nonfatal myocardial infarction in a patient as young as this

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IDIOPATHIC HEMOCHROMATOSIS

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Idiopathic hemochromatosis is a rare chronic disease characterized clinically by hepatomegaly, pigmentation of the skin, and diabetes mellitus, resulting from massive iron deposits in the tissues Herein reported is a case diagnosed by means of significant clinical and laboratory data and proved at autopsy

Report of a Case

A 56 year-old man was first seen April 25, 1958, complaining of progressive darkening of his skin, itching, marked fatigue, muscle aches, and impotence

He had had a complete diagnostic evaluation in 1948 elsewhere because of the pigmentation and a duodenal ulcer Adrenal cortical hypofunction (Addison's disease) was considered at that time because of the pigmentation, a 3 4-mg -per-24-hour 17-ketosteroid excretion, and a normal fasting blood sugar level The patient's history was otherwise normal, except that he had had a heavy alcohol intake prior to 1950 There was no history of anemia, excessive iron intake, or repeated blood transfusions Family history was noncontributory

Physical examination revealed an asthenic, darkly pigmented man who appeared older than his stated age The liver was firm, enlarged, and nontender, extending 3 fingerbreadths below the right costal margin The spleen was enlarged to 3 fingerbreadths below the left costal margin The testicular structures were softer and smaller than normal The remainder of the physical examination gave negative findings

He was hospitalized April 27, 1958, with a presumptive diagnosis of hemochromatosis The routine blood and urine examinations gave normal findings except for lymphocytosis of 56% Complete electrolyte studies and study of the blood urea nitrogen level showed normal findings Repeated measurements of fasting and postprandial blood sugar levels showed them elevated up to 390 mg % Tests of liver function revealed normal alkaline phosphatase, thymol turbidity, and bilirubin values but 11% sulfobromophthalein (Bromsulfalein) retention The albumin-globulin (A-G) ratio was reversed, with a normal total protein value Since his prothrombin times ranged between 27 and 47%, a biopsy of the liver was not performed The radioiodine rose bengal test indicated a marked depression of the cell function of the liver The iron binding capacity of the serum was 100% saturated at 180 mcg % Radioactive iron studies showed a normal iron utilization and plasma iron clearance rate A series of tests of the upper gastrointestinal tract revealed an old deformity of the duodenal bulb, hepatomegaly, and splenomegaly His chest x-ray showed normal findings The electrocardiogram showed low-voltage and non-specific T-wave changes in leads 1, aVL, and across the precordium A biopsy specimen of the skin had characteristic hemosiderin deposits, and the bone marrow showed excessive iron deposition on staining with Turnbull blue He was regulated on lente insulin and a diabetic diet and was dismissed from the hospital on May 18, 1958

As an outpatient he had five weekly 500-cc phlebotomies, and his hemoglobin level dropped from 14 to 11 6 Gm There was a lighter color to his skin, but he continued to complain of increasing weakness, fatigue, and muscle cramps in his legs On June 25, 1958, he developed abdominal distention with ascites

He was readmitted to Presbyterian Hospital on June 29, 1958, in order to evaluate the possibility of his adrenals being involved by the generalized disease process It was found that the 17-ketosteroids and 17-hydroxycorticoids were low, and that after ACTH there was no increase in the ketosteroids but an eight-fold increase in the 17-hydroxycorticoids The administration of ACTH produced a striking improvement in his general well being, the next day he was up and around, and his strength was much improved A test dose of 3 Gm of calcium versenate given intravenously was found to increase his 24-hour urinary iron excretion 15-fold from 1 64 to 23 71 mg Patient was again sent home and followed on an outpatient basis with weekly phlebotomies, but he had to be rehospitalized on Aug 12, 1958, because of weakness, confusion, and uncontrollable diabetes On this last admission his blood sugar level was 390 mg %, and he appeared cachetic, mildly acidotic, and chronically ill His diabetes was controlled with 60 units of U-80 lente insulin Four days after this admission he developed gastrointestinal bleeding and went into hepatic coma He was treated with fluids administered intravenously and was tapered off cortisone The gastrointestinal bleeding subsided spontaneously He was digitalized because of recurrent attacks of paroxysmal nocturnal dyspnea, orthopnea, and rales at both bases Despite large amounts of vitamin K, his prothrombin time remained at about 30% He continued to do poorly and died Sept 17, 1958, from a massive gastrointestinal hemorrhage

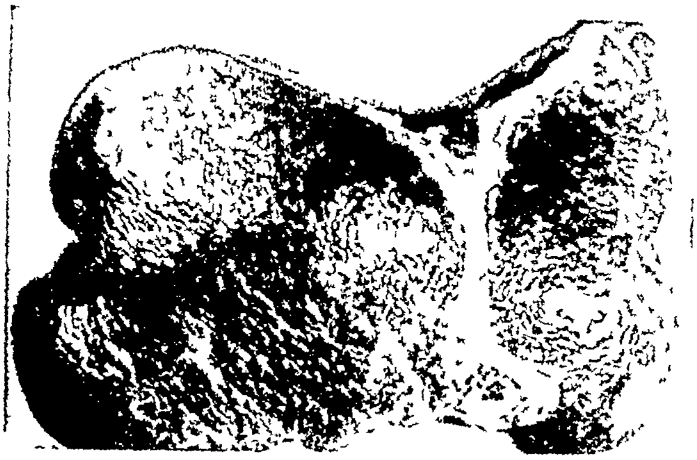

Fig 1 —Gross photograph of liver showing hobnailed surface of cirrhosis

Pathology

Autopsy revealed a well-developed man with a generalized bronzed discoloration of the skin and marked edema of the lower extremities extending up to the groin The right and left pleural cavities contained 900 and 500 cc respectively and the peritoneal cavity 3,000 cc of a clear, dark yellow fluid The heart weighed 456 Gm with thickening of the left ventricular anterior wall to 18 mm The coronary arteries were widely patent Examination of the pulmonary vascular tree revealed the smaller arteries to be occluded by thrombi The liver weighed 1,760 Gm and had a distinct yellowish tan color and a nodular hobnailed surface (fig 1) Sectioning revealed a nodular pattern interlaced with a shiny white fibrous tissue The hepatic artery was occluded by a thrombus The spleen weighed 450 Gm, was soft, and on sectioning revealed irregular areas consistent with infarctions The splenic artery was occluded by a thrombus near the terminal portion The pancreas was largely replaced by fat The pancreatic artery was occluded by thrombus (fig 2) Adrenals presented indistinct demarcation between cortex and medulla The testicles were small and the seminiferous tubule pattern indistinct No bleeding point was found in the gastrointestinal tract, but there were numerous distended veins along the mucosal surface of the esophagus and stomach, and the entire intestinal tract was moderately filled with dark red blood

Microscopically the heart presented focal areas of fibrosis and diffuse deposits of pigment within the myocardial fibers with focal accentuation This pigment stained blue with Turnbull's blue iron stain The sections of lung presented marked congestion with many areas of infarction The spleen showed a large area of infarction, congestion, and iron deposits within the walls of the veins and collagenous tissue The architecture of the liver was destroyed by dense fibrosis around the portal triads within which was seen marked bile duct proliferation and lymphocytic infiltration Heavy deposits of hemosiderin were present in the fibrous tissue, and Kupffer and hepatic cord cells (fig 3) The pancreas consisted only of a few small aggregates of acini and occasional islets and all contained deposits of hemosiderin Focal heavy deposits of pigment were seen in the zona glomerulosa of the adrenal (fig 4) The epithelial cells of the collecting and proximal convoluted tubules of the kidney contained hemosiderin Testes presented increased connective tissue, atrophy of the seminiferous tubules, and almost complete loss of spermatogonia Hemosiderin deposits were present in the Leydig cells The esophagus had numerous varicosities,

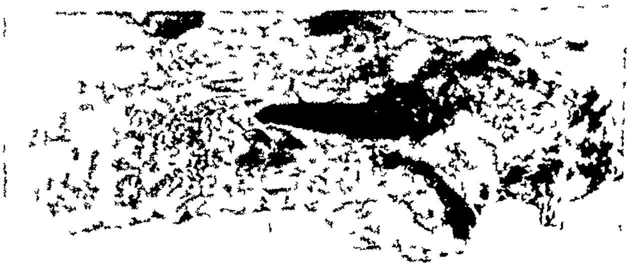

Fig 2 —Gross photograph of pancreas showing only a few pancreatic lobules within dense fibrous tissue Thrombus in pancreatic artery is centrally located

and the mucosa of the gastrointestinal tract contained hemosiderin deposits The lymph nodes were also markedly involved with hemosiderin deposits The bone marrow had an excessive amount of hemosiderin

Comment

The first case of hemochromatosis was described by Trousseau in 1865, and the name hemochromatosis was given to the disease in 1889 by Von Recklinghausen It has been observed once in about 7,000 hospital deaths and once in about 20,000 hospital admissions [1] In England where iron deficiency is common the incidence of hemochromatosis is low, while in Bantu natives where iron deficiency anemia rarely occurs the incidence of iron deposition is high Idiopathic hemochromatosis occurs about 10 times as frequently in men as in women, presumably due to the fact that the average woman loses 10 to 15 Gm of iron through her menses, pregnancy, and lactation during her lifetime It is a disease occurring in the fifth and sixth decades Hemochromatosis may occur as a familial disorder, and there are instances where two or more members of the same family had the disease, proved histologically [2]

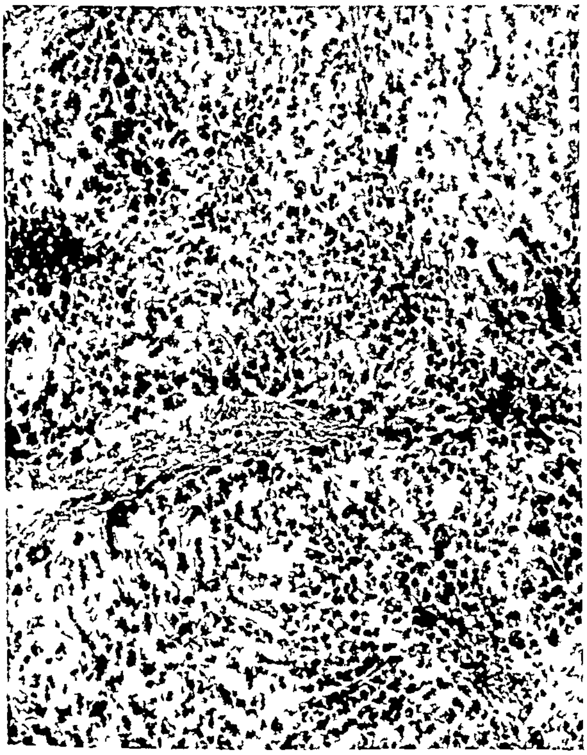

Fig 3 —Liver with heavy hemosiderin deposits in fibrous tissue and Kupfer and hepatic cord cells, Turnbull s blue stain (× 200)

Dietary factors may play a part, and, in a person with an increased capacity to absorb it, an increased iron intake over many years can cause hemochromatosis [3] Iron absorption is accelerated in both idiopathic hemochromatosis and iron deficiency anemia [4] Granick has proposed that anemia may be the cause of the excessive iron absorption [5] The high incidence of hemochromatosis in the Bantu natives in South Africa apparently is based on the high iron intake in the diet [6] Reduction of the phosphate content of the diet in experimental animals results in increased iron absorption [7] Pyridoxine deficiency has resulted in excessive iron absorption in animals [8] Kinney has demonstrated increased absorption of iron in dogs if the pancreatic duct is ligated [9]

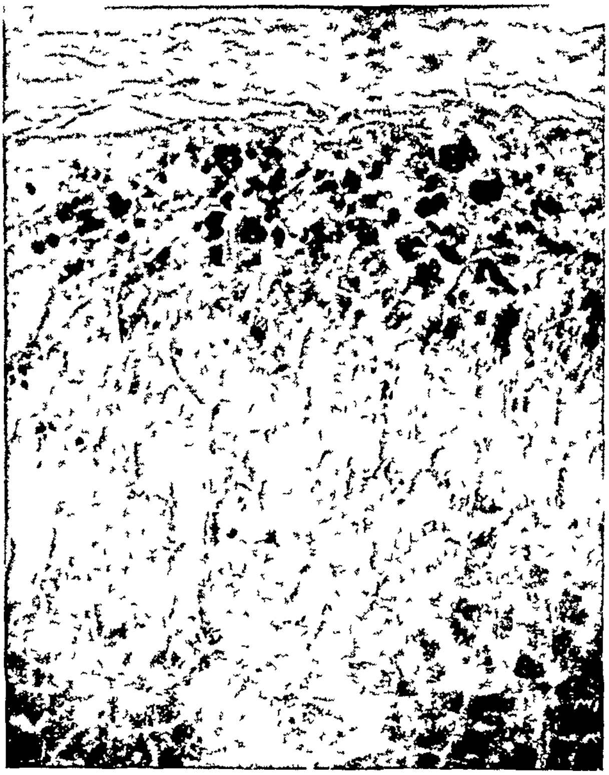

Fig 4 —Adrenal presenting heavy hemosiderin deposits in zona glomerulosa, Turnbull's blue stain (× 100)

Iron absorption is increased in idiopathic hemochromatosis as determined by iron absorption studies [10] The specific abnormality in the absorption mechanisms in idiopathic hemochromatosis is not known The plasma iron concentration is almost invariably above 150 mcg % and is commonly nearly saturated The plasma iron turnover (clearance) as determined by radioiron (Fe^{59}) is slow as compared to normal

The most common presenting symptoms are tiredness, weakness, malaise, loss of weight, and loss of libido Skin pigmentation is common, usually generalized, and of a slate gray or bronze color Diabetes with hepatomegaly, skin pigmentation, and hypogonadism should always suggest hemochromatosis The leading cause of death in hemochromatosis is congestive heart failure or cardiac arrhythmias attributed to myocardial hemosiderosis with secondary myocardial damage Peripheral neuritic pains in the extremities may be present with associated cramps, hyperesthesias, and tenderness

The diagnosis of hemochromatosis is established by demonstrating excessive deposits of iron with secondary organ damage Differential diagnosis must include adrenal cortical hypofunction, neoplastic disease such as lymphoblastoma, and Laennec's cirrhosis Twenty-nine per cent of the cases in Finch's series of hemochromatosis had a history of alcoholism [2a] There seems to be a definite association of alcoholism with Laennec's cirrhosis and hemochromatosis The present patient under discussion had a long history of alcoholism

Treatment at present consists of the removal of excess body iron and supportive treatment of the secondary organ damage Balfour has established that the iron storage in a patient with hemochromatosis is 25 Gm and that it would require about two years of weekly phlebotomies to deplete this iron storage in a patient with hemochromatosis [11] As hypoproteinemia develops, as it did in this case, it would seem advisable to replace the plasma after each phlebotomy The plasma iron will return to normal as the tissue iron stores are depleted by repeated phlebotomies A decreased skin pigmentation, reduction in the insulin requirements, and improvement in the cardiac and liver functions have also been observed with repeated phlebotomies [12] Dietary restriction of iron and attempts to reduce the iron absorption by making the iron insoluble in the colon with phosphates have been unsuccessful in treatment The chelating agent, edathamil calcium-disodium, may increase the urinary excretion of iron several fold, as occurred in this case, but it does not appear to provide a significant enough increase for therapeutic purposes [13]

The adrenal glands showed marked hemosiderin deposition in the zona glomerulosa in this case There have been other reports in the literature of adrenal cortical involvement from excessive hemosiderin deposits [14] The prognosis is generally poor, and the principal causes of death are hepatic coma, cardiac failure, hematemesis, and hepatoma

Summary

A case of idiopathic hemochromatosis with secondary involvement of the skin, liver, pancreas, adrenals, and myocardium has been presented The clinical and pathological findings have been discussed The use of a chelating agent, edathamil calcium-disodium, increased the urinary excretion of iron 15-fold, but this additional amount was not considered of therapeutic value Steroids were of temporary benefit in this case, presumably because the patient had adrenal cortical involvement from excessive hemosiderin deposits Repeated phlebotomies to remove the excess iron from the tissue stores, together with supportive treatment of the secondary organ damage in the liver, pancreas, adrenals, and myocardium, remain the most rational treatment To date there is no method available to alter the specific abnormality in the absorptive mechanism in idiopathic hemochromatosis The case presented failed to respond to present methods of treatment because of the irreversible secondary organ damage at the time the diagnosis was first recognized

1875 York (6) (Dr Dines)

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PROLONGATION OF THE P-R INTERVAL AS A MANIFESTATION OF THYROTOXICOSIS

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and
Joseph J Rupp, M D , Philadelphia

The cardiovascular manifestations of thyrotoxicosis such as tachycardia, palpitations, and increased pulse pressure are well known In some instances of thyrotoxicosis chest roentgenograms show straightening of the left cardiac border which simulates the roentgenographic pattern seen in patients with auricular enlargement [1] Likewise, in patients with hyperthyroidism a variety of electrocardiographic changes have been described These include [1] sinus tachycardia, auricular fibrillation, increased amplitude of R-II, and increased duration of the QRS complex [1] However, the more recent reports of the electrocardiographic changes in thyrotoxicosis, while stressing the above changes, do not report any alterations in the P-R interval [2]

Our interest in changes in the P-R interval in the electrocardiograms of patients with thyrotoxicosis was stimulated by the question of whether a patient with thyrotoxicosis, straightening of the left cardiac border on chest roentgenogram, sinus tachycardia at a rate of 126 and a P-R interval of 0 26 seconds had intrinsic heart disease as well as hyperthyroidism The straightening of the left cardiac border and sinus tachycardia were not unexpected in the thyrotoxic patient, but the prolonged P-R interval was disturbing since the P-R interval usually decreased with increasing heart rate and when prolonged is usually indicative of intrinsic heart disease [1]

Review of Electrocardiograms of Thyrotoxic Patients

In order to assess the significance of the P-R interval change we reviewed the electrocardiograms of 76 thyrotoxic patients, none older than 50 years and none of whom had a history of heart disease or clinical evidence of cardiac insufficiency No patient had been treated with digitalis preparations or quinidine Each patient had the classical signs and symptoms of thyrotoxicosis as well as an elevated protein bound iodine level, 24-hour thyroidal accumulation of I^{131}, and basal metabolic rate

The electrocardiograms of all patients showed sinus tachycardia, and in five the P-R interval was increased above 0 22 seconds, with a cardiac rate greater than 100 per minute In four of the five patients the P-R interval had returned to normal when the patients were rendered euthyroid The fifth patient has only begun treatment and follow-up observations are not yet available (see the table)

These observations of the prolongation of the P-R interval in some patients with thyrotoxicosis without evident heart disease not only confirm the earlier observations of Krumbhaar,[3] and of Goodall [1] but they also point out that the abnormal P-R interval returns to normal when the thyrotoxicosis is controlled

In reviewing the electrocardiograms of 104 patients (of the same age group) with sinus tachycardia and no clinical evidence of heart or thyroid disease we found one patient to have a full P-R interval of 0 20 seconds and one a prolonged P-R interval of 0 23 seconds Thus the incidence of prolonged P-R interval in our series of thyrotoxic patients (5/76) is significantly greater than our control series (2/104)

Electrocardiographic Findings in Five Patients Treated for Thyrotoxicosis

	While Thyrotoxic		When Euthyroid	
Age Yr	Rate/Min	P R Interval	Rate/Min	P R Interval
29	126	0 26	80	0 16
41	128	0 24	78	0 18
31	120	0 24	82	0 18
42	118	0 22	74	0 16
37	106	0 24		

The P-R interval prolongation with sinus tachycardia, in the absence of other electrocardiographic alterations which occurred in these patients and which reverted to normal when the thyrotoxicosis was controlled, is probably a reflection of the cardiac response to thyrotoxicosis rather than the result of intrinsic heart disease Awareness that these electrocardiographic changes may occur in hyperthyroidism in the absence of other evidence of heart disease and that they revert to normal when the thyroid disease is controlled may help in determining the presence of intrinsic heart disease in patients with thyrotoxicosis

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From Jefferson Medical College Hospital and Lankenau Hospital

DEATHS

Aarons, Edward Flynn Jr , Pensacola, Fla , Meharry Medical College, Nashville, Tenn , 1917, chief of staff, Our Lady of Angels Hospital, associated with the Escambia General Hospital, Sacred Heart Hospital, and Baptist Hospital, where he died May 30 aged 67, of myocardial infarction

Arguelles, Fernando Luis Ⓜ El Paso, Texas, Universidad Nacional Autonoma de Mexico Faculted de Medicina, Mexico, D F , 1905, died June 11 aged 81, of cerebral hemorrhage

Bartlett, James Curtis, Ontario, Ore Willamette University Medical Department, Salem, 1910, veteran of World War I, died in Boise May 22, aged 84, of complications following fracture of the right humerus and right femur

Becker, Frank Charles, Chicago, Medical College of Indiana, Indianapolis, 1896, served on the staffs of the Grant Hospital and the Alexian Brothers Hospital, where he died June 17, aged 91, of bronchopneumonia

Bernard, Emil Lawrence Ⓜ Springfield, Ill , Northwestern University Medical School, Chicago, 1909, member of the American Academy of General Practice, past-president of the Sangamon County Medical Society, veteran of World War I, associated with St John's Hospital, died June 6, aged 75, of paralysis agitans

Brandon, William Alvin, Carbondale, Ill , College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1908, associated with the Doctors and Holden hospitals, died June 12, aged 79, of arteriosclerotic heart disease

Brown, James Dowling Ⓜ Youngstown, Ohio, University of Michigan Medical School, Ann Arbor, 1928, past-president of the Mahoning County Medical Society, associated with the Youngstown Hospital Association, served as editor of the *Bulletin of the Mahoning County Medical Society,* died June 12, aged 58, of coronary thrombosis

Brown, Warwick Thomas Ⓜ Vice Admiral, M C , U S Navy, retired, Washington, D C , born in Parkerville, Kan , in 1890, Kansas Medical College, Medical Department of Washburn College, Topeka, 1913, specialist certified by the American Board of Internal Medicine, joined the Navy in 1917 and served during World War I as assistant surgeon of the Fourth Marine Brigade in France, during World War II was commanding officer of the First Medical Battalion and surgeon of the First Marine Division on Guadalcanal, later commanded the Naval hospitals at Quantico, Va , and at St Albans N Y , assigned to the Fifth Naval District in Norfolk when he retired to accept the position as administrator at Emergency Hospital, retired from the U S Navy on April 1, 1952, in 1956 appointed first administrator of the Washington Hospital Center and retired in March, 1959, among his military decorations were the Legion of Merit, Gold Star, and Bronze Star, died May 16, aged 70, of coronary occlusion

Burns, Robert M , St Paul, University of Minnesota College of Medicine and Surgery, Minneapolis, 1905, associated with the Midway Hospital, St Luke's Hospital, Mounds Park Hospital, and St Joseph's Hospital, where he died June 6, aged 81, of hemorrhage, cerebral and gastrointestinal

Caldwell, Lorenzo D , Mathias, W Va , Baltimore Medical College, 1893, served on the staff of the Rockingham Memorial Hospital in Harrisonburg, Va , died in Timberville, Va , June 4, aged 91, of cancer of the intestine

Chan, Hubert, San Leandro, Calif , University of Louisville (Ky) School of Medicine, 1956, interned at the San Joaquin General Hospital in French Camp and the Highland–Alameda Hospital in Oakland, captain in the U S Air Force retired, died in the Letterman General Hospital, San Francisco, May 16, aged 29, of granulocytic leukemia

Clements, John Harold, Juneau, Alaska, University of Nebraska College of Medicine, Omaha, 1933, interned at the Nebraska Methodist Episcopal Hospital and Deaconess Home in Omaha and the King County Hospital Unit number 1 in Seattle, member of the House of Delegates of the American Medical Association in 1950, past-president of the Juneau Medical Society, associated with St Ann's Hospital, where he died June 3, aged 57, of myocardial failure

Coleman, James Meredith Ⓜ Austin, Texas, born Nov 30, 1906, Baylor University College of Medicine, Dallas, 1930, specialist certified by the American Board of Pediatrics, member of the American Academy of Pediatrics, interned at St Louis City Hospital, where he was assistant resident, resident and chief medical resident, member of the board of directors of the Travis County Medical Society, of which he was past-president, formerly chief of communicable diseases and later director of maternal and child health of the Texas State Department of Health, served as director of health and welfare for Travis and Bastrop counties and city health officer, chief of pediatrics service at Brackenridge and Seton hospitals, member of the com

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Ⓜ Indicates Member of the American Medical Association

mittee on medical history and the editorial advisory committee for the *Texas State Journal of Medicine*, died in St Louis June 2, aged 53, of a heart attack

Conn, Hugh Irving Ⓜ Newman, Ill , Bennett Medical College, Chicago, 1915, veteran of World War I, for many years president and member of the school board, in June, 1958, the citizens of Newman held a "Dr Conn Day Celebration" which honored him for 37 years of medical and public service to the Newman community, past-district-governor of Kiwanis International, on the staff of Jarman Hospital in Tuscola, died in Tuscola June 9, aged 69, of coronary thrombosis

Crosby, Edward P , Stevens Point, Wis , Wisconsin College of Physicians and Surgeons, Milwaukee, 1904, past-president of the Ninth Councilor District Medical Society, charter member of the staff of St Michael s Hospital, where he died May 24, aged 83, of arteriosclerotic heart disease

Davis, Harry Harmon Ⓜ Rolla, Mo , University of Arkansas School of Medicine, Little Rock, 1937, member of the American Academy of General Practice, veteran of World Wars I and II, on the staff of the Phelps County Memorial Hospital, died June 9, aged 64, of multiple cerebral thrombi and diabetes

Dickinson, Gyrdie Willie, Winthrop, Mass , University of Vermont College of Medicine, Burlington, 1905, served as port medical officer for the United Fruit Company in Boston, for many years town and school physician of Winthrop, for eight years president of the staff of Winthrop Community Hospital, died in the Whidden Memorial Hospital, Everett, May 29, aged 84, of arteriosclerotic heart disease

Donaldson, Aubrey Albert, Trenton, Tenn , Memphis (Tenn) Hospital Medical College, 1903, died May 11, aged 83, of coronary occlusion

Drew, George Francis, Devils Lake, N D , University of Minnesota College of Medicine and Surgery, Minneapolis, 1900, for many years city health officer, state senator from Ramsey County for eight sessions, died in the Mercy Hospital June 8, aged 85, of diabetes

Ewer, John Norton Ⓜ Oakland, Calif , University of California School of Medicine, San Francisco, 1927, specialist certified by the American Board of Obstetrics and Gynecology, fellow of the American College of Surgeons, veteran of World War II, a member of the staffs of Merritt and Peralta hospitals, died June 2, aged 60, of carcinoma of the pancreas

Fleet, Carl William, Houston, Texas, Baylor University College of Medicine, Dallas, 1937, veteran of World War II, died in the Hermann Hospital June 4, aged 48, of acute renal insufficiency

Garmon, Clyde Neville, Bessemer, Ala , Birmingham Medical College, 1914, died in the Lloyd Noland Hospital, Fairfield, May 6, aged 68, of cirrhosis

Harner, Clyde Ernest Ⓜ Leucadia, Calif , University of Colorado School of Medicine, Denver, 1920, specialist certified by the American Board of Ophthalmology and of the American Board of Otolaryngology, fellow of the American College of Surgeons, veteran of World War II, died in the U S Naval Hospital in San Diego June 3, aged 65, of portal cirrhosis

Hayward, Vincent Sumner Ⓜ Elmhurst, N Y , Columbia University College of Physicians and Surgeons, New York City, 1908, past-president of the Bronx County Medical Society, veteran of World War II, served with the U S Veterans Administration, on the staff of the Goldwater Memorial Hospital, New York City, died in the Boulevard Hospital, Long Island City, June 12, aged 75, of pulmonary edema

Heimburger, LeRoy Francis, Springfield, Mo , born in St Louis in 1889, St Louis University School of Medicine, 1912, specialist certified by the American Board of Dermatology, member of the American Academy of Dermatology and Syphilology, for many years a medical missionary in China, from 1921 to 1934 associate professor and head of the department of dermatology and syphilology at the Shantung Christian University in Tsinan, China, past-president of the Greene County Medical Society and editor of its bulletin, 1947-1948, associated with the Burge Hospital, Medical Center for Federal Prisoners, Springfield Baptist Hospital, and St John's Hospital, where he died May 27, aged 70, of ventricular fibrillation and arteriosclerotic heart disease

Heinz, Lawrence Henry, South San Francisco, Calif , University of Minnesota Medical School, Minneapolis, 1941, interned at St Joseph's Hospital in St Paul, veteran of World War II, died in Burlingame March 24, aged 44

Herrick, John Claudius, La Jolla, Calif , Denver and Gross College of Medicine, 1903, served on the faculty of his alma mater, died April 28, aged 81, of cerebral arteriosclerosis and thrombosis

Hicks, Elizabeth Shreve Ⓜ San Francisco, University of California School of Medicine, San Francisco, 1937, interned at the University of California Hospital in San Francisco and the Baltimore City Hospitals, served a residency at the Hospital for Children and St Joseph s Hospital, died June 13, aged 50, when fire destroyed her cottage at Tiburon, Calif

Hinson, Eugene Theodore, Philadelphia, University of Pennsylvania Department of Medicine

Philadelphia, 1898, founder of the Mercy Douglass Hospital, where he died June 7, aged 86, of congestive heart failure

Holder, Charles Oakley Ⓜ Kalamazoo, Mich , Indiana University School of Medicine, Indianapolis, 1934, interned at the Highland Park (Mich) General Hospital, served a residency at the Kalamazoo State Hospital, where he was assistant medical superintendent, specialist certified by the American Board of Psychiatry and Neurology, member of the American Psychiatric Association, veteran of World War II, died May 26, aged 52, of acute coronary occlusion

Holsted, Albert Beeler, Temple, Okla , University of Arkansas School of Medicine, Little Rock, 1912, veteran of World War I, died in Wichita Falls, Texas, June 5, aged 70, following an operation for gallstones

Howell, Floyd Wayne Ⓜ Temple, Texas, Baylor University College of Medicine, Dallas, 1930, member of the American Academy of General Practice, associated with the King's Daughters Hospital and Scott and White Memorial Hospitals, died May 25, aged 56, of hepatitis

Howland, Bernard Union Ⓜ Portsmouth, Ohio, University of Louisville (Ky) School of Medicine, 1927, specialist certified by the American Board of Urology, member of the American Urological Association, fellow of the American College of Surgeons, veteran of World War II, associated with Portsmouth General Hospital, chief, department of urology, Mercy Hospital, where he died June 3, aged 58, of coronary occlusion

Jacobs, Harry J., Downey, Calif , University of Cincinnati College of Medicine, 1944, interned at the Cedars of Lebanon Hospital in Los Angeles, associated with the Rancho Los Amigos Hospital, served on the faculty of the College of Medical Evangelists, Loma Linda and Los Angeles, died in St Francis Hospital, Lynwood, May 26, aged 43, of acute myocardial infarction

James, Edward Dean Ⓜ Joplin, Mo , University of Arkansas School of Medicine, Little Rock, 1901, veteran of World War I, died May 28, aged 89, of coronary occlusion

Johnson, Malcolm Liddell, Paris, Texas, University of Texas School of Medicine, Galveston, 1935, veteran of World War II, served on the staff of the Sanitarium of Paris, division surgeon for the Frisco Railway, died May 30, aged 49

Kienholz, Leon Edward Ⓜ Ossining, N Y , University of Oregon Medical School, Portland, 1927, member of the American Academy of General Practice, veteran of World War I, formerly psychiatrist at Sing Sing Prison, on the staff of the Phelps Memorial Hospital, died June 8, aged 65, as the result of an automobile accident

Kile, James Bernard, Eddyville, Neb , Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1906, veteran of World War I, associated with the Good Samaritan Hospital in Kearney, died June 7, aged 77, of a heart attack

Killam, Franklin Harrison Ⓜ Greensboro, Ga , Tufts College Medical School, Boston, 1914, died in the Minnie Boswell Memorial Hospital May 21, aged 68, of acute cardiac failure and coronary infarction

Lane, Clayton Rogers, Santa Monica, Calif , University of Vermont College of Medicine, Burlington, 1914, veteran of World War I, member of the American Urological Association, on the staff of the Santa Monica Hospital, died June 5, aged 72, of myocardial infarction

Lawrence, John Vincent Ⓜ St Louis, Rush Medical College, Chicago, 1925, certified by the National Board of Medical Examiners, assistant physician at the Barnes Hospital, where he died June 12, aged 66, of carcinoma of the right lung with metastases

Lefferts, David Ⓜ New York City, Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin, Prussia, Germany, 1929, specialist certified by the American Board of Radiology, member of the American College of Radiology, associated with the Montefiore Hospital, died June 15, aged 64, of myocardial infarction, coronary sclerosis, and hypertension

Leveroos, Edward Herbert Ⓜ New Orleans, born in Superior, Wis , June 12, 1910, University of Minnesota Medical School, Minneapolis, 1940, interned at the Minneapolis General Hospital, president-elect of the Louisiana Hospital Association, secretary-treasurer of the Hospital Service Association of New Orleans, member of the American Association for the Advancement of Science and Alpha Kappa Kappa, colonel, U S Air Force Reserve, command surgeon for the 5th Fighter Command of the Army Air Corps during World War II, served as clinical director of the Veterans Administration Hospital in Hines, Ill , later became director, Division of Hospitals and Graduate Education, American Medical Association, director of the Ochsner Foundation Hospital, died June 19, aged 50

Light, Gertrude Underhill, Alcalde, N M , Johns Hopkins University School of Medicine, Baltimore, 1898, died in the Espanola (N M) Hospital May 24, aged 88, of arteriosclerotic heart disease

Lindley, Calvin Denton, Carrizo Springs, Texas, University of the South Medical Department Sewanee, 1901, at one time mayor of Carrizo Springs, died June 3, aged 81, of pyelonephritis

Lindsey, Laurence L, Hermosa Beach, Calif , College of Physicians and Surgeons, Los Angeles, 1909, served as mayor, veteran of World War I, died May 26, aged 80, of carcinoma of the prostate

McIntosh, Robert Kerr Jr, Tahlequah, Okla , University of Oklahoma School of Medicine, Oklahoma City, 1937, interned at the Good Samaritan Hospital in Portland, Ore , member of the American Academy of General Practice, veteran of World War II, served as county health officer, in 1958 named the Outstanding Alumnus of Tahlequah High School" and was selected as the 'Outstanding Citizen of Tahlequah' in 1959-1960, died May 29, aged 47, of coronary thrombosis

McKnight, Vernon Hastings, Elkton, Md , University of Maryland School of Medicine, Baltimore, 1910, on the staff of the Union Hospital, died June 5, aged 74, of coronary occlusion

McMillan, Thomas J, Milan, Ga , Hospital Medical College, Eclectic, Atlanta, 1911, died in the Telfair County Hospital, McRae, May 8, aged 69, of cerebral hemorrhage

Maged, Alan John, Suffern, N Y , University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1928, past-president of the Rockland County Medical Society, associated with the Tuxedo Memorial Hospital in Tuxedo Park and the Good Samaritan Hospital, on the board of the Lafayette Bank and Trust Company, died June 1, aged 58, of arteriosclerotic heart disease

Manson, Frank Melville Ⓜ Worthington, Minn , University of Minnesota College of Medicine and Surgery, Minneapolis, 1899, fellow of the American College of Surgeons, veteran of World War I, for many years served on the board of the public library, formerly county coroner, died June 10, aged 89, of bronchopneumonia

Mellone, John Anthony Ⓜ West Barrington, R I , Georgetown University School of Medicine, Washington, D C , 1933, interned at the St Joseph's and Charles V Chapin hospitals in Providence, Barrington police surgeon, veteran of World War II, died May 31, aged 52, of coronary thrombosis

Miller, Henry William, Brewster, N Y , born in Orillia, Ont , Canada, Nov 22, 1873, University of Toronto Faculty of Medicine, Toronto, Ont , 1895, member of the American Psychiatric Association and the Association for Research in Nervous and Mental Diseases, served as clinical director of St Elizabeth's Hospital in Washington, D C , from 1910 to 1914 superintendent of the Augusta (Maine) State Hospital, served as superintendent of Mountainbrook, formerly on the faculty of Columbia University College of Physicians and Surgeons in New York City, where he was associated with the Neurological Institute at the Columbia-Presbyterian Medical Center and the Vanderbilt Clinic, died June 22, aged 86, of cancer

Miller, Leon Wilbur, Honolulu, Hawaii, Yale University School of Medicine, New Haven, Conn , 1943, interned at St Vincent's Hospital in Jacksonville, Fla , served a residency at the Santa Barbara Cottage Hospital in Santa Barbara, Calif , and the Medfield State Hospital in Medfield, Mass , veteran of World War II, associated with the Hawaii Department of Health, died in Waimanalo May 15, aged 42, of myocardial failure

Mixson, William Daniel Ⓜ Waycross, Ga , Chattanooga (Tenn) Medical College, 1898, past-president of the Ware County Medical Society, veteran of World War I, served on the staffs of the King's Daughters' Hospital and the Ware County Hospital, for many years president of the First Federal Savings & Loan Association, died June 2, aged 90, of cerebral hemorrhage

Montgomery, Clarence V Ⓜ South Hill, Va , University College of Medicine, Richmond, 1905, on the staff of the Community Memorial Hospital, died June 4, aged 78, of heart failure

Moore, Frank Judson Ⓜ Beckley, W Va , Eclectic Medical College, Cincinnati, 1919, served as member and for one term president of the Raleigh County Board of Education, died in Beckley Hospital June 19, aged 77, of arteriosclerosis

Morton, Warren Ralph, Seattle, University Medical College of Kansas City, Mo , 1913, for many years practiced in Green, Kan , died May 31, aged 73, of pneumonia

Mosby, George Leroy, Lake Villa, Ill , Chicago College of Medicine and Surgery, 1915, veteran of World War I, associated with the Veterans Administration Hospital in Downey, where he died May 16, aged 76, of coronary thrombosis

Myers, Gordon Bennett Ⓜ Detroit, born in Detroit April 24, 1904, University of Michigan Medical School, Ann Arbor, 1927, specialist certified by the American Board of Internal Medicine, served an internship and residency at the City of Detroit Receiving Hospital, where he was later director of medicine, formerly a resident physician at the Peter Bent Brigham Hospital in Boston, served as professor and chairman of the department of medicine at Wayne State University College of Medicine, in 1958 in recognition of his "inspiring leadership' an annual senior award in his name was established by former students, member of the American Heart Association, Association of American Physicians, Central Society for Clinical Research, American Society for Clinical Investigation, New York Academy of Sciences, the Endocrine Society, Alpha Omega Alpha, and Sigma

Xi, fellow of the American College of Physicians, consultant in medicine, Veterans Administration Hospital in Dearborn, from September, 1958, until his retirement last October, was head of the university service in internal medicine at Harper Hospital, a 17-reel film on physical diagnosis was prepared by him, Dr Muir Clapper of Detroit, and Dr Frederick Margolis of Kalamazoo, wrote many medical papers and books on physical diagnosis and heart research, died in the Grace Hospital June 5, aged 56, of intraventricular cerebellar hemorrhage

Newcomb, Carmen Adams, Santa Monica, Calif, Washington University School of Medicine, St Louis, 1894, formerly assistant health officer with the Los Angeles Health Department, died June 12, aged 89, of gastrointestinal hemorrhage

Nicholson, Harold Earl Jr Ⓜ Wheeler, Texas, Baylor University College of Medicine, Dallas, 1942, veteran of World War II, on the staff of the Wheeler Hospital, died May 31, aged 43, of coronary occlusion

Parnell, Homer Sylvester Jr, West Columbia, S C, Vanderbilt University School of Medicine, Nashville, Tenn, 1939, interned at the Charity Hospital in New Orleans, where he served a residency, veteran of World War II, served with the Regional Office of the Veterans Administration in Columbia, died in Columbia May 30, aged 45, of coronary thrombosis

Polk, Mannie Arnold Ⓜ Chicago, University of Illinois College of Medicine, Chicago, 1923, member of the American Academy of General Practice, for many years associated with the Grant Hospital, where he died June 24, aged 62, of myocardial infarction

Privett, Lowell Bernard Ⓜ Boise, Idaho, born in Woonsocket, S D, Dec 3, 1900, Creighton University School of Medicine, Omaha, 1929, past-president of the Southwestern Idaho District Medical Society, member of the American Academy of Ophthalmology and Otolaryngology and the Aero Medical Association, specialist certified by the American Board of Ophthalmology, interned at Creighton Memorial, St Joseph's Hospital in Omaha, veteran of World War II, associated with St Alphonsus Hospital, where he served on the executive board, and St Luke's Hospital, died June 13, aged 59, of hypernephroma with multiple metastasis

Parrish, Robert Eunice Ⓜ San Antonio, Texas, born in 1891, Jefferson Medical College of Philadelphia, 1914, specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology, member of the American Academy of Ophthalmology and Otolaryngology and the American Broncho-Esophagological Association, past-president of the Bexar County Medical Society, past-vice-president of the San Antonio Ear, Eye, Nose and Throat Society, served in the regular Army, veteran of World War I, past president of the board of directors, Robert B Green Hospital, associated with the Nix Memorial, Baptist Memorial, and Santa Rosa hospitals, died May 29, aged 69, of coronary thrombosis

Quickel, John Cephas Ⓜ Gastonia, N C, University of Pennsylvania School of Medicine, Philadelphia, 1932, interned at the New Rochelle (N Y) Hospital, past-president of the Gaston County Medical Society, an eye, ear, nose, and throat consultant at the North Carolina Orthopedic Hospital, past president of the Rotary Club, died in the Garrison General Hospital May 16, aged 53, of myocardial infarction

Ratcliffe, Griffith John Ⓜ Philadelphia, Temple University School of Medicine, Philadelphia, 1926, veteran of World War II, associated with the Germantown Dispensary and Hospital, died June 17, aged 60, of acute coronary occlusion

Robinson, Robert Edwin, Waverly, Iowa, State University of Iowa College of Medicine, Iowa City, 1894, on the staff of St Joseph Mercy Hospital, where he died May 31, aged 90, of ruptured aneurysm of abdominal aorta

Royal, Kent Tyler, North Brookfield, Mass, Harvard Medical School, Boston, 1919, chairman of the board of health, medical examiner of the Ninth Worcester District, for many years school physician, chief of staff at Mary Lane Hospital in Ware, where he died June 1, aged 68, of coronary disease

Schwarzbart, Samuel, Syracuse, N Y, Friedrich-Wilhelms-Universitat Medizinische Fakultat, Berlin, Prussia, Germany, 1924, member of the American Academy of General Practice, on the courtesy staff of the Crouse-Irving Hospital, where he died May 31, aged 62, of cerebral hemorrhage

Shea, Daniel Edward Ⓜ Hartford, Conn, born in Hartford Jan 18, 1893, Loyola University School of Medicine, Chicago, 1917, member of the American Urological Association, fellow of the American College of Surgeons, veteran of World War I, formerly associated with the U S Public Health Service, served as director of the bureau of venereal diseases of the Hartford Department of Health, on the staff of St Francis Hospital, where he died May 31, aged 67, of cerebral hemorrhage and diabetes

Siscovick, Milton Ⓜ Baltimore, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1935, member of the American Academy of General Practice, veteran of World War II and the Korean War, died May 31, aged 48, of arteriosclerotic heart disease

Smith, George, Pilot Rock, Ore., Rush Medical College, Chicago, 1921, formerly mayor, for many years a member of the school board, died May 31, aged 66, of injuries received in an automobile accident near North Platte, Neb.

Swartzlander, Henry Carver, Clearwater, Fla., Creighton University School of Medicine, Omaha, 1912, died in Calgary, Alberta, Canada, May 14, aged 71, of congestive heart failure.

Swihart, Leonard Francis, Elkhart, Ind., Indiana University School of Medicine, Indianapolis, 1924, veteran of World War I, served as treasurer of the school board, member of the staff of the Elkhart General Hospital, died May 28, aged 61, of coronary occlusion.

Thoma, Raymond J., Chicago, St. Louis College of Physicians and Surgeons, 1918, examining physician for Selective Service during World War II, a member of the staff of the Evangelical Hospital, medical director of Pettibone Mulliken Corporation, died June 7, aged 69, of carcinoma of the bladder.

Toomey, Francis Elmer, San Diego, Calif., Creighton University School of Medicine, Omaha, 1926, veteran of World War II, for many years chief autopsy surgeon of San Diego County, on the staffs of the Mercy and Quintard hospitals, served as editor of the *Bulletin of the San Diego County Medical Society,* died in the U. S. Naval Hospital June 7, aged 60, of cirrhosis of the liver.

Ullum, Robert Lloyd, Liberty Center, Ohio, University of Cincinnati College of Medicine, 1955, interned at St. Vincent's Hospital in Toledo, associated with S. M. Heller Memorial Hospital, Napoleon, died June 9, aged 40, in a plane crash at Findlay.

Vail, George Alvin, Lawrenceburg, Ind., Indiana University School of Medicine, Indianapolis, 1941, member of the American Academy of General Practice, associated with Margaret Mary Hospital in Batesville, Good Samaritan Hospital in Cincinnati, and Dearborn County Hospital, resigned from the regular Navy Jan. 7, 1948, accidentally drowned June 3, aged 45, when his boat overturned in the Ohio River.

Veltman, Henriette Ⓜ Paris, Tenn., Chicago College of Medicine and Surgery, 1910, died in the Henry County Hospital May 28, aged 79, of hypertensive heart disease.

Walker, George Heman, Lincoln, Neb., born in Weeping Water June 25, 1881, University of Nebraska College of Medicine, Omaha, 1908, member of the American Academy of General Practice and of the Association of Life Insurance Medical Directors of America, for many years secretary of the Lancaster County Medical Society, of which he was past-president, served as instructor in anatomy at his alma mater, veteran of World War I, medical director of the Lincoln Liberty Life Insurance Company and the Pioneer Life Insurance Company, on the staffs of the Bryan Memorial and Lincoln General hospitals, died June 2, aged 78, of myocardial failure and postoperative hemorrhage.

Weisblum, Maurice, Collingswood, N. J., University of Pennsylvania Department of Medicine, Philadelphia, 1907, specialist certified by the American Board of Physical Medicine and Rehabilitation, consultant in physical medicine and rehabilitation at the Albert Einstein Medical Center, Southern Division in Philadelphia, where he was associated with the Philadelphia General and Jewish hospitals, died in Our Lady of Lourdes Hospital, Camden, June 14, aged 74, of coronary occlusion.

Welsh, Thomas William, Calistoga, Calif., Northwestern University Medical School, Chicago, 1903, veteran of World War I, died in the Veterans Home of California–Nelson M. Holderman Memorial, Veterans Home, June 8, aged 81, of myocardial insufficiency.

Whallon, Arthur James, Richmond, Ind., University of Cincinnati College of Medicine, 1911, past-president of the Wayne County Medical Society, veteran of World War I and held several service medals from the American, British, and French armies, served on the board of health, associated with the Reid Memorial Hospital, died June 1, aged 73, of pulmonary emphysema.

Wilhelm, Joseph Victor, Arlington, Ore., George Washington University School of Medicine, Washington, D. C., 1908, died in The Dalles June 5, aged 82, of cerebral vascular accident.

Wilkinson, George E., Alton, Ill., Washington University School of Medicine, St. Louis, 1898, served as a member of the board of education, on the staffs of the Alton Memorial and St. Joseph's hospitals, died in the Alton Memorial Hospital May 28, aged 91, of encephalomalacia.

Wisener, Guthrie Howard, Richmond, Ind., Indiana University School of Medicine, Indianapolis, 1917, fellow of the American College of Surgeons, past-president of the Wayne-Union Counties Medical Society, of which he was treasurer, veteran of World War I, served on the staffs of the Reid Memorial Hospital, Earlham College, Richmond State Hospital, and the Smith-Esteb Memorial Hospital, died in the Methodist Hospital, Indianapolis, May 18, aged 74, of bacteremia and meningitis.

Zaratt, Jacinto Ⓜ San Juan, P. R., University of Pennsylvania Department of Medicine, Philadelphia, 1897, died March 20, aged 85, of myocardial failure and generalized arteriosclerosis.

FOREIGN LETTERS

FRANCE

Griseofulvin—At a meeting of the Société Médicale des Hôpitaux de Paris, R Degos and co-workers reported a series of 144 patients with tinea capitis who had been hospitalized for several months and treated with epilation by irradiation Having replaced radiotherapy with griseofulvin since 1959, the authors observed, through repeated microscopic examination, that changes occurred in the areas affected by tinea since the first days of the antibiotic treatment

Examination of hair samples showed two distinct parts in the hair the proximal part was perfect and healthy, while the distal part was heavy with parasites The non-parasitic areas measured about 3 mm on the 10th day of the griseofulvin therapy and 7 mm on the 20th day In patients with trichophytic and microsporic tineas the healthy areas measured about 4 mm on the 20th day The griseofulvin treatment could be interrupted when the parasitic part was sufficiently removed from the scalp so that the hair could be cut off

Of 37 patients with favus due to Trichophyton schoenleini, 36 were cured without recurrence after three weeks of treatment One patient, who had been unsuccessfully treated for 20 years, recovered from generalized favus after two months

Hadida from North Africa reported dramatic recoveries in 47 patients who had favus and who were treated with this drug Of 27 patients with trichophytic tinea 25 were cured after the first course of treatment, and 2 patients who had recurrences were cured after a second course In another series of 76 patients (26 infected with Microsporum audouini and 50 with Microsporum canis), 69 recovered completely Seven had recurrences (two infected with Microsporum audouini and five with Microsporum canis), but they were cured after a second course of treatment

Recurrences of tinea caused by Microsporum animalis and considered benign are brought about by autocontamination due to the persistence of the affected hair or the fact that the affected hair is encased by layers of myriads of spores, each one a potential source of autocontamination In order to prevent recurrences from autocontamination and transmission of parasites from patient to patient, the authors combined the new treatment for tinea capitis with daily soapy washing followed by rubbing with iodinated salicylated alcohol They also advised that the patients shave or have a close haircut on the plaques and surrounding areas at the beginning of the treatment and again around the 20th day

Griseofulvin was also used to treat 80 patients who had onychomycosis and other cutaneous infections Superficial mycosis and hairless scalp due to trichophytons were cured within three weeks Palmar and plantar mycoses required treatment for two or three months because of the thickness of the epidermis at these levels Good results were also recorded in eczematous dermatitis On the other hand, there were failures in patients with pityriasis versicolor and cutaneous infections caused by Candida albicans Patients with trichophytic onychomycosis were cured within four to seven months of treatment, even those whose disease was of 40 years' duration

The adult dosage of griseofulvin was 1 Gm daily, given orally Children received an initial dosage of 0 75 Gm daily, later reduced to 0 50 Gm Tolerance to the drug was excellent Repeated hemograms and renal function tests performed on 80 patients showed no ill effects

Experiments with Alcotest—At a meeting of the Académie Nationale de Médecine in February, R Monod described a type of inhalator which allows a biochemical test of alcohol intake by examining the air expired by the subject This test of alcoholism in patients involved in accidents eliminates the need for blood samples Of 231 tests performed with the inhalator, the results were positive in 131 and negative in 100 (The test does not react to the small quantities of alcohol present after taking one cocktail or two glasses of wine at mealtime) Comparison of the results obtained with the alcotest and blood-alcohol determination showed that both tests gave identical results

GERMANY

Treatment of Leukopenia and Hypercholesteremia—H A Nieper (*Med Welt*, no 7, p 379, 1960) stated that the metabolic role of magnesium has been unrecognized until recently It activates trophotropic cell enzymes and thereby improves epithelial growth This increase in chemical and morphological cell assimilation should also be the cause of the leukocyte-activating effect of magnesium, described by Delbert Nieper tried to influence leukopenia by giving magnesium ascorbate to patients who had leukopenia caused by massive doses of chloramphenicol, busulfan, or thyreostatic and antipyretic drugs The magnesium was expected to effect an increase in leukocytes except in leukopenia due to treatment with thiouracil derivatives In the latter case the reduction in thyroxin level is associated with impairment of cell respiration, and activation of trophotropic ferments by magnesium is limited

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The items in these letters are contributed by regular correspondents in the various foreign countries

A 28 year-old woman who had worked several years in a uranium mine and who had severe marrow depression was given weekly injections of copper detoxin subcutaneously and daily injections of magnesium Marrow findings and blood coagulability returned to normal Leukopenia, after chloramphenicol treatment, is no serious complication and usually disappears of its own accord When the magnesium ascorbate is given together with the chloramphenicol, leukopenic reactions fail to occur The magnesium salts of nicotinic acid and dehydrocholic acid were also tried

Elderly patients with multiple sclerosis were given tablets containing magnesium nicotinate and magnesium dehydrocholate in the proportion 6 1 Blood cholesterol levels were determined before treatment, after seven days, and then at greater intervals The average reduction in serum cholesterol level was 30% after seven days in those who had elevated levels before treatment An especially good result was obtained in a 35-year-old man who had intermittent claudication and cardiac infarction and who complained of frequent stenocardiac symptoms The serum cholesterol level can also be lowered by therapy with theobromine-magnesium-oleate, but improvement does not occur in less than two months with this drug, while with magnesium nicotinate it starts immediately Even nicotinic acid alone may lower the cholesterol value, but magnesium nicotinate is cheaper and more effective

Local Treatment with Liver Extract—W K Meyerhoff of Borstel (*Hautarzt* 11 86, no 2, 1960) cleaned cutaneous ulcers with 3% hydrogen peroxide, then applied a plastic foil dressing soaked with liver extract diluted with saline solution in the proportion 1 4 The surrounding area was covered with Unna's paste, and the dressing was covered with lawn to produce a moist chamber This was left for 24 hours A 69-year-old woman who had cutaneous ulcers, myocardial weakness, and marked anasarca was almost pain-free at the first changing of the dressing and her ulcers were fairly clean After 48 hours the ulcers were perfectly clean Edema persisted even after complete healing of the ulcers Within a fortnight, after granulation had come up to skin level, epithelization began Complete cure was achieved in 21 days Within the atrophic glossy skin healthy tissue formed in spite of the persisting edema

As a control test three ulcers were treated with liver extract parenterally and three others locally None of the six patients stayed in bed The locally treated ulcers healed but the others did not until they were also treated locally Undiluted liver extract did not give better results One man with chronic osteomyelitis following a compound fracture of the tibia had an ulcer that had resisted treatment for more than 12 years He was completely cured within 14 months of application of liver extract without bed rest The diabetic ulcer in another patient completely healed within 19 days, although his diabetes was not controlled The treatment was also used in four patients with nonspecific postoperative fistulas, some of them of 18 months' duration Secondarily healing wounds also responded well The effect was most impressive in burns Even third-degree burns healed with minimal scarring

INDIA

Histamine and Tropical Eosinophilia—R D Ganatra and co-workers (*Indian J M Sc* 14 328, [April] 1960) made quantitative estimations of the blood histamine level in 48 subjects (14 with no disease, 24 with tropical eosinophilia, and 10 with bronchial asthma) In nine patients with tropical eosinophilia, estimations were made before and after two injections of diethylcarbamazine, each of 6 mg per kilogram of body weight given intramuscularly at an interval of two days The mean total eosinophil count in normal persons was 662 per cubic millimeter, and level of histamine was 3 2 mcg per 100 ml

The patients with tropical eosinophilia had predominantly respiratory symptoms and a peripheral eosinophil count of more than 2,000 per cubic millimeter The mean total eosinophil count in these patients was 10,409 cells per cubic millimeter and the mean histamine level was 18 mcg per 100 ml The corresponding values in patients with bronchial asthma were 9,958 and 22 4 Thus, the histamine levels in patients with tropical eosinophilia and those with bronchial asthma were significantly higher than those in normal persons The difference between the blood levels of patients with the two diseases was statistically insignificant The post-treatment blood levels of histamine were significantly lower than the pretreatment levels in patients with tropical eosinophilia The mean total eosinophil count fell from 13,922 to 2,355 and the histamine level from 20 0 to 4 8 mcg per 100 ml Analysis of the values in patients with tropical eosinophilia showed a trend toward correlation between eosinophilia and histamine levels, although there was no functional relationship between the two The authors concluded that blood histamine levels are usually elevated in patients with tropical eosinophilia, although sometimes such a rise did not occur No correlation was seen between the severity of symptoms and the blood levels of histamine The post-treatment fall in the level of blood histamine and relief of symptoms were marked whenever the pretreatment level had been high Both eosinophilia and blood histamine levels were affected by diethylcarbamazine The difference between the levels of asthmatics and of patients with tropical eosinophilia was not statistically significant As elevated histamine levels in patients with asthma were usually attributable to allergy, the similar elevation in patients with tropical eosinophilia might be due to the same factor Only one of these conditions is associated with tropical eosinophilia, and the authors therefore believed that the rise in blood histamine and eosinophilia could be independent effects of allergy The probability of finding an elevated histamine level associated with an increased eosinophil count in tropical eosinophilia is great, as the two seemed to be correlated

Cancer of the Uterine Cervix—T K Ghosh (*J Obst & Gynec India* 10.287 [March] 1960) compared the results in patients with stages 1 and 2 carcinoma of the uterine cervix five years after treatment by radiotherapy and by surgical extraperitoneal lymphadenectomy and radical vaginal hysterectomy The cure rate with the former was 46 4% and with surgery 65 6% The operation was done in two parts In the first part the pelvic lymph nodes were removed en masse through an extraperitoneal approach The second part consisted of removal of the uterus, its adnexa and parametrial tissue by the vaginal route The case fatality rate in 216 patients operated on by this technique was 3 6% With continued use of this technique the mortality decreased significantly and there was not a single death among the last 55 patients operated on Postoperative complications and fistula formation were rarely met with, although the operation involves mobilization of the ureters, urinary bladder, urethra, and rectum There were no instances of ureteric fistula and only two patients, who had previously received radium treatment, developed a vesicovaginal fistula The presence of a fibroid tubo-ovarian mass, or ovarian cyst, did not affect the operation On the other hand, when present these could be treated more easily during the operation because of prior ligation of uterine and ovarian vessels in the first part of the operation

The advantage of the operation is that all detectable lymph nodes can be removed effectively Five-year survival rates of patients with cancerous and noncancerous lymph nodes showed that the prognosis was much better in the latter group Supervolt radiotherapy was given to all whose lymph nodes showed cancer cells and those with parametrial metastases The author concluded that the operation satisfies all conditions of surgical treatment of cancer cervix It is reasonably safe even for obese patients or those who are comparatively poor surgical risks It has the further advantage of rehabilitating the bladder

Recurrent Dislocation of the Shoulder—A K Saha (*Indian J Surg* 22 66 [Feb] 1960) used a new operative technique on 10 patients with recurrent dislocation of the shoulder The detached labrum during the initial dislocation fails to reattach even after prolonged rest and the tendon of the subscapularis muscle becomes elongated with consequent loss of power There is obvious muscle incoordination when the optimum power of the subscapularis muscle is lacking To correct this, the author transferred the latissimus dorsi tendon with intact nerve and vascular supply to a point exactly opposite the attachment of the subscapularis on the posterior aspect of the upper end of the humerus During abduction this muscle then was able to help the subscapularis to roll the humeral head backward and to prevent its slipping forward The synergistic action of this muscle was checked electromyographically during the later stages of abduction of the arm overhead

Of the 10 patients treated by this technique, one had bilateral dislocation and one was previously treated by Bankart's operation without success Following operation, plaster immobilization was maintained for six weeks in the zero position Special care was taken to check this position because the head tended to deviate if the humerus did not keep strictly in the scapular plane with consequent postoperative subluxation and fixation of the head in the new position All the patients successfully operated on were performing their normal duties when last seen, and one of them, a wrestler, had gone back to his profession without any recurrence The quickest recovery of function in the series was three weeks after removal of plaster The method is entirely extra-articular and the author found it easier and less time consuming than the classical Bankart's operation Rehabilitation is comparatively quicker with no depreciation of any movement including external rotation Complications were minimal barring those due to bad positioning after the operation

Transaminase Activity in Liver Disease—Vanikar and Bhatt (*Indian J M Sc* 14 344 [April] 1960) determined the values for GOT (serum glutamic oxalacetic transaminase) and GPT (serum glutamic pyruvic transaminase) in patients with hepatic diseases and compared these with the results of some common liver function tests Other workers have shown that both values are elevated in hepatic disease, and that GPT has an additional advantage as it is not appreciably altered by acute myocardial infarction Elevation of these two has been considered to indicate liver cell destruction and not liver cell dysfunction, and thus differs from other liver function tests In this study these values were determined in 17 patients with infective hepatitis, 9 with portal cirrhosis, 2 with obstructive jaundice, 3 with biliary cirrhosis, and 1 with carcinoma of the liver

The authors conclusively showed the usefulness of including GOT and GPT measurements for assessing liver function in patients with infective hepatitis No particular relationship was noticed between GOT and GPT levels, either of these two could have a high value initially, but GPT took longer to come down to normal than GOT In later stages of hepatitis, therefore, GPT determination would be of greater help and more specific For complete recovery, both levels should come back to normal Rapid fluctuations in serum transaminase activity in proportion to the extent of liver cell necrosis were observed in contrast to other liver function tests In surgical jaundice, the values for GOT and GPT were not so high as they were in infective hepatitis and came down in about three days after obstruction was relieved

To differentiate between obstructive and hepatocellular jaundice, the authors recommended estimation of serum transaminase activity as well as serum alkaline phosphatase In biliary cirrhosis also, the transaminase activity was never so high as in patients with infective hepatitis in spite of the seriousness of the condition in chronic cases Of the nine patients with portal cirrhosis, five had jaundice There was no difference in the serum transaminase values in patients who had jaundice and those who did not In the patients with carcinoma of the liver, a high GOT level was present and probably indicated the onset of active necrosis supervening on a carcinomatous process Thus serum transaminase levels in chronic liver diseases were normal or only a little raised, while other liver function tests were abnormal The rise was found during the active phases of the necrotizing process, the height of the transaminase activity represented active liver cell damage and was not related to the seriousness of the condition or to the functional damage of liver The values were of particular help in studying the progress of patients who had infective hepatitis

NORWAY

Reserpine for Schizophrenia —Dr A Gravem and co workers (*Tidsskr norske laegefor*, May 1, 1960) made a follow-up study of 72 male patients in a mental hospital, 58 of whom suffered from some form of schizophrenia and all of whom had been treated with reserpine The mean duration of their disease was 15 years (range from 1 to 42) The initial dose of the drug was usually 5 mg daily, gradually increased according to individual needs to about 10 mg daily The dosage might be held at this level for weeks or months When no further improvement was noted it was gradually reduced to a maintenance dose of 1 to 4 mg daily Of the 72 patients, 12 had died and 21 had been discharged The action of the drug may be only symptomatic, but its effects may be dramatic in the patient, the character of whose disease may be changed, with catatonic phases passing off and the impression gained that a door has been opened to a world of realities

The drug has been given for over four years to some patients and the mean duration of the treatment was between two and three years At the time of the follow-up examination varying degrees of improvement could be claimed in 89%, and marked improvement in 50% The best results were achieved in those with catatonic schizophrenia Results were less good in those with hebephrenic schizophrenia and poorest in those with organic psychoses The results did not seem to depend on the duration of the disease The drug therapy should be given a trial of at least three months before it is abandoned for want of an early response In some patients no improvement could be claimed before it had been given continuously for one to two years When successful, the drug should be continued indefinitely, because discontinuance or a reduction of dosage is usually followed by a relapse

Sulfadimethoxine for Urinary Infections —On the surgical side of the Rikshospital in Oslo, sulfadimethoxine was used to treat a series of 71 patients suffering from various infections of the urinary tract The initial dose, according to Dr Mathisen (*Tidsskr norske laegefor*, May 15, 1960) was 1 Gm daily for two days followed by a maintenance dose of 0 5 Gm daily This long-acting drug is still demonstrable in the urine five days after the administration of a single dose of 1 Gm It takes about 35 hours for the concentration of the drug in the blood to be reduced to half that of its original highest level, whereas this time is reduced to about 10 hours in the case of relatively briefly acting sulfonamides

In only one patient did the drug give trouble in the form of nausea and vomiting, affecting a patient known already to be allergic to various other drugs This reaction subsided promptly when the drug was discontinued Otherwise it was well tolerated, and it had no toxic effect even when it was given continuously to several patients for more than five months There was no evidence of accumulation even after prolonged medication The effects were better than those achieved by the prolonged administration of briefly acting sulfonamides In the many patients with chronic pyelonephritis in whom the drug fails to render the urine sterile, the patient may become symptom-free and be rid of pain and bouts of fever Freedom from symptoms with sterile urine was achieved in 63% of the patients, and in 25%, relief was obtained in spite of persistence of bacteriuria Hence, it was concluded that this drug is useful for patients requiring continuous treatment for months or years

Sulfadimethoxine for Skin Diseases —At Ullevaal hospital, sulfadimethoxine has been given to a series of 57 patients, 21 of whom were outpatients Two tablets were given by mouth on the first day and one tablet daily thereafter Dr R Fodstad (*Tidsskr norske laegefor*, May 15, 1960) continued this treatment for 3 to 19 days (average 7 9) Among the 39 patients suffering from pyoderma were 31 whose lesions healed in a few days Healing occurred within five weeks in 8 of the 12 patients who had acne Satisfactory healing was achieved in 10 patients in whom Staphylococcus aureus had been found resistant to sulfonamides in vitro Two of five patients suffering from dermatitis herpetiformis responded favorably, and a patient with lymphogranuloma inguinale showed complete recovery after 14 days No untoward reactions were observed About 9,000 patients have already been treated with this drug, and slight side-effects were reported in less than 2%

UNITED KINGDOM

Anorexia Nervosa.—Dally and Sargent of St Thomas's Hospital, London (*Brit M J*, June 11, 1960), reported a series of 20 patients who had anorexia nervosa and who were treated by a new method, and a control series of 24 patients who were treated by other methods With the new method, patients were put to bed at the start of treatment and kept there until they regained near-normal weight (depending on their previous weight, height, and age) Thus food intake could be supervised, and risks of using large doses of the prescribed drugs in debilitated patients were minimized Chlorpromazine was given by mouth, starting with 150 mg a day and increasing by 75 mg a day to the limit of the patient's tolerance As much as 1 Gm a day has been required by the most difficult patients, one of whom weighed only 72 lb (32 7 kg)

If signs of paralysis agitans appeared and increased, small doses of benzhexol hydrochloride were added Modified insulin therapy was also begun at once, the dose starting with 5 units and progressively increasing until the patient perspired visibly and became drowsy Then the insulin treatment was stopped and a large meal was given Precautions were taken throughout the day to avoid occurrence of late hypoglycemia None of the patients so treated reacted with abnormal sensitivity, though this has been thought by some to be a theoretical objection to the use of insulin in treating anorexia nervosa The average morning dose used in the series was 60 units (range from 40 to 80, according to individual sensitivity)

Early in the treatment a light diet was given It included frequent fortified milk drinks and was steadily increased from 1,500 to 4,000 calories a day In this way abdominal discomfort, a common cause of complaint in the early stages of treatment, was reduced to a minimum The patient's confidence was gained, and reassurance was constantly given, but no attempt was made to uncover psychological problems or to deal with them until the patient's weight was nearly normal Then the drug dosages were reduced, and the patient was allowed up A week later, provided the patient was still eating satisfactorily, she was discharged home Attempts were made to study patients for at least a year, and supportive psychotherapy with the patient in a remission seemed valuable in preventing relapse A maintenance dose of chlorpromazine also helped to prevent relapse in some patients

Most patients began to gain weight almost a once when treated with the combination of chlorpromazine and insulin Some of the large initia weight increase was undoubtedly due to wate retention, but this was regarded as a favorable sign, and it was usually accompanied by increasing cheerfulness and more ready acceptance of treatment The underlying worry about eating often persisted, but no longer frightened the patient to the point of self-starvation

It seemed to be the combination of insulin and chlorpromazine that was so effective, for neither drug given alone, nor in insufficient doses, produced as good results If either chlorpromazine or insulin therapy was stopped before the weight was satisfactory, or if the patient was allowed up and about too soon, she was likely to relapse Putting the patient back to bed and readministering either drug in proper amounts quickly reversed this tendency With the patient totally confined to bed and given careful nursing, no complications were encountered However, late hypoglycemia could occur if the patient were left too long unobserved, and the hypotensive effects of chlorpromazine in such large doses in emaciated persons could be severe if the patient were allowed up too early

The Presidential Address—Sir Arthur Porritt's address at the annual meeting of the British Medical Association in June at Torquay was delivered in the presence of the retiring President, Prince Philip, Duke of Edinburgh Sir Arthur, who is Chairman of the Porritt Committee, observed that more and more governments are accepting responsibility for part or all of the common health This calls for a working relationship between physicians and the government Modern medical science has changed the nature of history by adding a new dimension to it It is a tragedy that the conception of equal partnership between government and the medical profession for the praiseworthy purpose of ensuring the well-being of the nation should have failed so dismally

The National Health Service has not worked out as it should have, and the original idea of partnership has been displaced by an employer-employee relationship Much of the blame for this is due to the failure of the Civil Service to cope with an agency which is essentially concerned with people, not things When one appreciates that those people are patients and doctors, joined in the NHS in a peculiarly personal relationship, it becomes evident that an impersonal governmental department is not the best mechanism through which to administer it The NHS should be administered by an independent corporation What such a scheme implies is the disbursement and application of public moneys by an independent body, without the intervention of departmental machinery and without the need for a Minister to be answerable to Parliament for the day to day conduct of the service This would lift medicine out of the realm of party politics, an influence which has bedeviled the NHS from its inception

Alternative to National Health Service Shelved—When the British Medical Association's 128th annual meeting opened, a scheme for an alternative to the NHS, prepared by its Amending Acts Committee, was shelved This was a tacit admission that Britain's 40,000 doctors in the NHS were content with the new pay scale offered by the government Five hundred copies of the alternative scheme had been brought from London, but as only a handful of doctors voted in favor of publication it remains confidential This may mark the end of attempts to introduce an alternative to the NHS

Spiritual Healers—Five hundred doctors attending the British Medical Association's annual meeting voted unanimously for the exclusion of spiritual healers from Britain's 3,500 hospitals "Treatment in the National Health Service," said Mr H Langston, chairman of the Central Consultants and Specialists Committee, "is the province of doctors in the employment of hospital boards and committees and of no other body" Recently, 257 of 450 management committees agreed to allow members of the National Federation of Spiritual Healers to enter the wards The federation has 2,500 members Mr Langston said "The aid and assistance of authorized priests and ministers of religion in their proper sphere is welcomed by us all, and great is the comfort and assistance they can give to many a patient Their cooperation assists us in our work with the patient and in his recovery"

The self-styled spiritual healers are mostly spiritualists, and have nothing in common with ministers of religion The patient in hospital has the right to ask whom he wishes to visit him including so-called spiritual healers, but if he wishes to receive treatment from a "healer," it should be made plain that while he is in hospital no treatment of any sort can be allowed which is not authorized by the doctor who is caring for him The doctors' attitude was supported by the Churches Council of Healing, the Free Church Federal Council, and the Royal College of Nursing

Dr Doris Odlum, psychiatrist, and a BMA member of the Churches' Council, said that spiritual healers worked by establishing a mediumistic connection with dead persons They claimed thereby to receive guidance on the treatment to be employed Medical treatment and spiritual healing combined would produce a very confused and divided state of mind in a patient He would not know whom to believe in or which treatment to have confidence in It would make an impossible situation for doctors and nurses Even if healers did not go into a trance they would disturb other patients in the ward

Psychiatrists Urged to Quit Tower of Babel—Leading psychiatrists, in a mood of self-criticism at the British Medical Association's annual meeting, admitted that they are almost as mixed up as the people they seek to help Their president, Dr E B Strauss, said they dwelt in a new tower of Babel The trouble is the extraordinary language they use The main objective of words is to communicate something Words should have universal meaning It is unfortunate that clinical psychiatrists have not been able to evolve a common language Nearly meaningless and mischievous diagnostic labels are used Psychiatrists have lagged behind other branches of medicine in clarity of expression The result has been chaos It is time that such vague terms as neurasthenia be dropped

Control of Drugs—New drugs should be controlled until proved safe, according to the Royal College of Nursing This would be better than the present practice of listing them as dangerous only when they have been found so The College's views were given in a memorandum submitted to a Committee of the Parliament

The conclusions reached by the College were based on recommendations of a group that included hospital matrons, nurses, pharmacists, and hospital administrators The College urged that the British Pharmacopoeia Commission give new drugs an official name with minimal delay Many new drugs have appeared on the market, and there is often a great time lag before an official name was issued

The public should be encouraged more forcefully to destroy leftover medicaments A standard code of practice regarding the custody, administration, and checking of dangerous drugs should be adopted A general practitioner should always be required to record the administration of a dangerous drug Physicians should more often have the name of a drug included on the label of the patient's container All dangerous drugs should be clearly labeled The College recommended that hospital prescriptions for dangerous drugs should be legibly signed in full, and the practice of signing initials only should be abandoned The usual practice of keeping a register of dangerous drugs in the wards and departments of a hospital should be made a legal requirement Drugs should not be administered in hospital without a written prescription, except in a real emergency

CORRESPONDENCE

CHLORAMPHENICOL

To the Editor —The report of the Council on Drugs in The Journal, April 30, 1960, reviewing the occurrence of blood dyscrasias associated with the administration of chloramphenicol (Chloromycetin), was interesting, in seven years, 91 cases of pancytopenia occurred in patients to whom the drug had been given I am certain that we are all aware, thanks to the publicity provided by the manufacturer, of the potentiality of such a reaction This drug, which continues to be one of the most useful of the antibiotics is not, according to the Council on Drugs, to be used prophylactically, in trivial infections, or in infections in which other, less dangerous (kanamycin? ristocetin?) antibiotics may be used effectively

It would seem that a follow-up report is due to the medical profession (and to Parke-Davis) from the Council on Drugs, to wit, in exactly how many cases of pancytopenia had this medication been given in the usual manner (250 to 500 mg every six hours for five or six days might be considered an average course), and in what number had the medication been given for a protracted period of time? If there are any patients who were otherwise hematologically normal and who were given only a few doses with dire results we should know about it and reserve the medicament for the desperately ill If such is not the case, chloramphenicol should not have such an undue onus placed on it and we should be advised that it can be safely administered, if used in a proper and sensible manner

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The statement which appeared in The Journal was intended as a reminder, since information had reached this office that this antibiotic was being misused on occasion by some members of the profession The reason it was stated that the drug should not be used prophylactically, in trivial infections, or in infections in which other, less dangerous antibiotics may be used effectively is that reports received by the registry indicate that some physicians had used the drug for such conditions as the common cold, sore throat, and tonsillitis, which might be considered trivial and would not warrant the use of a product possessing potentiality for hematopoietic toxicity As far as other antibiotics are concerned, we have had fewer reports indicating as high a morbidity and mortality as with this product The literature does not contain as many reports of blood dyscrasias as have been attributed to this drug

No "follow-up report" is possible since the information received by the registry comes from a wide variety of sources and may represent only a segment of the actual incidence of blood dyscrasias associated with the use of this drug Consequently, it would be difficult to make any analysis of the type suggested by Dr Ellerbroek There is no doubt that this drug can be used safely in conditions where it is indicated if it is used properly—Ed

SIR CHARLES S SHERRINGTON

To the Editor —In an editorial on Fernel in The Journal, April 23, page 1938, reference is made to "Sir Charles S Sherrington of Cambridge" Is this about the same as referring to "Walter B Cannon of Yale"? Sherrington was professor at Oxford, Cannon at Harvard

Singer's "Short History" (1928) speaks of Sherrington of Oxford (p 309) Fulton's "Selected Readings" (1930) speaks of Sherrington at Oxford (p 284) Actually, he did much of his work at Liverpool, however, perhaps we should not confine such a distinguished man to any one town

Austin Lamont, M D
Philadelphia

This letter struck me with remorse I immediately ran for help The editorial had been reviewed by a professor of medical history, and no comment was made of a false location of Sherrington's affiliations The Kinsman Professor of Neurologic Research at the University of British Columbia, who is familiar with many details of Sherrington's life, and the editor of the *British Medical Journal* were consulted next The replies are as follows

"You did not make clear in your letter who is attempting to beat you up for calling Sherrington a Cambridge man, but, of course, the fact is that he graduated from Cambridge and served at Oxford only from 1913 to 1935 While this is the period of his greatest fame, probably his greatest work was done prior to coming to Oxford

"He was found watching the dog fights in the sky during the Battle of Britain perched on top of the Royal College of Surgeons, which as you know later received a direct hit Sherrington was taken to Cambridge and was looked after with truly filial care by the Master of his former College and by his colleagues there You should not back down, therefore, on calling Sherrington a Cambridge man for whatever reason '—William C Gibson, M D , Vancouver, B C , Canada

'About Sherrington—he entered Caius College, Cambridge, in 1880 Sherrington, in fact, was a Cambridge man His first paper was written in collaboration with J M Langley He was appointed Professor of Physiology at Liverpool in 1895, and subsequently migrated to Oxford Personally, I think that you are right in saying that Sherrington would have liked to be identified with Cambridge If you turn up the *British Medical Journal* of Nov 22, 1947, when we celebrated his 90th birthday, you will see that T Graham Brown referred to Caius College, Cambridge, as Sherrington s real Alma Mater''—Hugh Clegg, M D , London

On subsequent occasions I shall probably refer to the distinguished neurophysiologist by hedging as follows "Sherrington of Cambridge, Liverpool, Oxford, and Cambridge '—Ed

OUR SENSE OF HUMOR

To the Editor—In my opinion, the outstanding fault with the medical profession today is that it views the world and all its (medical) problems too seriously THE JOURNAL has misplaced our sense of humor Paramount, as proof of this, is the decline in the number of humorous cartoons and Tonics and Sedatives and in the quality of the few jokes that are currently published in THE JOURNAL

Let us, for the sake of medicine and the patient, restore humor interlude to medical journals Let us instill again the idea that all plans for legislating medicine are a joke, and all we have to do is laugh and say "All right, you guys, do it without us!' Let us return to a laughing state wherein we find humor in life and medicine

For heaven's sake, keep our sense of humor whetted by putting more humor (and not some of the so-called serious articles which are humorous) into the pages of THE JOURNAL If you do not want to make dyspeptics of all of us, give us something to laugh at

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This is precisely what we are attempting to do in Satire' The contributions are coming in slowly The field is open —Ed

TUBERCULIN TEST

To the Editor—There is an omission in the interesting article in THE JOURNAL, May 14, page 129, by Stein and Hetherington, "Fifteen Years' Experience with the Tuberculin Test' This article reviews the history of the improvement of this test, its modification by the use of purified protein derivative (PPD), and the standardization of both 'old tuberculin' (OT) and PPD for use in man The authors cite the method of Lewis and Aronson (*Am Rev Tuberc* 7 404 [Aug] 1923), whereby equal amounts of a standard and an unknown tuberculin are injected intradermally and the size of the reactions compared, and state that It is this method, modified for human subjects, that is now used to compare the potency of newly made tuberculin with a standard-strength tuberculin"

This statement may have been sufficient some years ago, but since 1947 the National Institutes of Health have required all OT or PPD that is subject to interstate commerce to be tested for potency by serial titration in sensitized guinea pigs against a reference standard preparation The reference standard is, in turn, based on the international standard which has been in existence for almost 30 years Furthermore, the NIH requirements are so designed that with care in testing it is possible to detect differences of as little as 20% between the preparation under test and the reference standard Thus, all OT or PPD distributed in the United States in the past 13 years has been subjected to a test of potency much more precise than the older method Admittedly, there are some discrepancies between guinea pig reactions and human reactions However, the test strengths of OT or PPD ordinarily used in man differ tenfold or more, whereas the official test of these products is normally made in serial twofold dilutions Thus, the routine application of such a test, measuring each new preparation against an internationally adopted standard, should give assurance that the OT or PPD on the market possesses a much higher degree of uniformity than one would infer from reading the article in question

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ACCURATE TERMINOLOGY

To the Editor—In THE JOURNAL, May 28, page 445, Dr R U Whipple calls the term medical examiner for a forensic pathologist "confusing and misleading to the general public" To his reasons could be added that nearly all medical licensing boards in the United States are called "State Board of Medical Examiners," although their members are not forensic pathologists He asks for help on the semantics of this problem

New technical terms should be of obvious and unequivocal meaning, they should not suggest anything but this meaning, and they should not contain elements of two different languages “Mortology has only the vague meaning of “science of death”, it could refer to the theological aspects of immortality as well as to forensic medicine It resembles the word “mortician” (itself a gem of kakoneologopoiesis), and it is a Latin-Greek hybrid I offer the term “medicolegal examiner ’ It is no profound change from the present term but avoids its drawbacks “Criminomedical examiner’ might be better, because the term “medicolegal” is used more and more for aspects of medical practice related to civil law “Crime pathologist” might be the best

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THE STEMMA OF HARVEY

To the Editor—In order to relieve the confusion created by the note on the Stemma of Harvey in The Journal, June 11, page 711, I would like to point out that the description by Ruth Fox is not correct, as the candle is really a torch and is not entwined by “a snake” but by two snakes, which is an important item in the old discussion about whether the caduceus should have one or two snakes

Bruno Gebhard, M D
Cleveland

No more on “The Stemma of Harvey ”—Ed

MAIL-ORDER DRUGS

To the Editor—I am concerned about the many drugs which are now being offered to physicians by mail-order companies at lower prices than are paid for such drugs when they are made by ethical pharmaceutical companies and sold through prescription pharmacies Prednisone and prednisolone especially are thus advertised and distributed for 1/10 to 1/15th of the charge for these corticoids made by ethical concerns

These cheap products have no insignia on them indicating the manufacturer I assume that most of them are being made out of the United States or by some manufacturer who does not wish to stand behind the effectiveness of the hormone I have given these corticoids to selected allergic patients whose financial status is very limited Unfortunately, the resultant control of the allergy has been less than that brought about by similar doses of such hormones made by ethical companies In some cases, no relief has occurred at all

These low-cost, apparently inferior corticoids, I believe, have been largely responsible for the congressional inquiry into the cost of such products and other drugs Thus the criticism of charges of ethical companies has not been entirely justified If these inexpensive corticoids are allowed to be sold they should be carefully tested by the Council on Drugs or by a government agency They should, moreover, have an imprinted insignia identifying the manufacturer who is responsible for their effects

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INCOMPATIBLE BLOOD TRANSFUSIONS

To the Editor—With reference to the question in The Journal, Jan 2, page 119, regarding the largest amount of incompatible blood that has been given a patient who has survived the resulting reaction and to Dr Crossley’s observation in The Journal, June 4, page 612, I would like to call attention to the article, “Transfusion Reactions and Their Treatment, Especially with the Artificial Kidney,” by Barlas and Kolff, in The Journal, April 25, 1959, page 1969 In this article, the authors reported a case in which a patient survived the transfusion of seven pints of incompatible blood with the aid of four treatments with the artificial kidney The volume of incompatible blood transfused, though important, is probably only one of several vital factors that determine recovery in these cases

Maurice W Black, M D
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PREANESTHETIC MEDICATION WITHOUT NARCOTICS

To the Editor—In The Journal, June 18, page 797, appeared the paper “Preanesthetic Medication Without Narcotics” by Dr George Wallace of Brooklyn Physicians who give the paper only a cursory glance may conclude that one should employ a drug such as racephedrine hydrochloride or amphetamine phosphate as a preanesthetic agent in accord with Dr Wallace’s recommendations that one use a sympathomimetic agent He recommends such drugs as atropine and scopolamine, which are not sympathomimetic but parasympatholitic Some of the effects of the parasympatholitic drugs are similar to those of the sympathomimetic drugs, but for pharmacological purposes the proper words should be used in the proper places

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MEDICAL FILM REVIEWS

Side to Side Portacaval Shunt 16 mm , color, sound, showing time 26 minutes Prepared by John L Madden, M D New York Produced in 1960 by and procurable on rental ($10) or purchase ($150) from Sturgis Grant Productions, Inc 322 East 44th Street, New York 17

The patient is a 52-year-old woman with a history of recurrent episodes of hematemesis Her history revealed excessive intake of alcohol for a period of 30 years, and studies confirmed the diagnosis of esophageal varices The author prefers and demonstrates a long right subcostal incision, this, he states, is preferable to the thoraco-abdominal incision The gallbladder is aspirated, then closed for purposes of exposure The surgical anatomy of the structures surrounding the foramen of Winslow is depicted very well The common duct is isolated and retracted, and the portal vein and inferior vena cava are mobilized and prepared for side-to-side anastomosis The author emphasizes the importance of identification of both renal veins The anastomosis is accomplished with the use of nonabsorbable suture material in conjunction with a Beck-Potts clamp used on the vena cava and two angulated Potts clamps placed on the portal vein The technique of the anastomosis is amplified by excellent color illustrations Following the anastomosis, the portal pressure is reduced from 403 to 283 mm H_2O The technique is good, and it is refreshing to see a modern surgeon emphasize the usage and importance of finger dissection The author states that an esophagram taken three months later was normal It would have been a nice addition and far more convincing if this roentgenogram had been included in the film The photography and narration are excellent, and this film is recommended for general surgeons, vascular surgeons, and residents interested in this type of surgery

Current Trends in the Clinical Management of Diabetes 16 mm , color, sound, showing time 32 minutes Produced in 1959 by Medical Radio and Television Institute, New York for and procurable on loan from the Upjohn Company Kalamazoo, Mich

In this film, Dr Peter H Forsham and Dr Henry Dolger discuss the management and treatment of diabetes, and Dr Paul Dudley White explains the cardiovascular complications associated with the disease Dr Forsham discusses and stresses the problem of good control in diabetes mellitus and its relation to the degenerative complications, namely, retinopathy and renal involvement The questions raised and comments made by Dr Forsham's associates are concise and practical Illustrations of dental, optical, and renal complications are shown, and the importance of adequate diabetic control prior to and after an operative procedure is well demonstrated by a case presentation Dr Dolger's statements as to the importance of the orally administered compounds in maintaining consistent good control of the diabetic state may be optimistic, since sufficient trial time has not elapsed to determine their value Dr White's statements regarding statistics on vascular and cardiac deaths are well taken, since he points out that with good control the longevity of the diabetic is almost that of the nondiabetic This motion picture has been produced in color, utilizing a number of television production techniques which add to the viewer s sense of immediacy and reality during panel discussions and make the presentation interesting Photography and sound recording are very good It is recommended for internists, general practitioners, and house staff officers and would also be helpful to the senior medical student

Community Mental Health 16 mm, black and white, sound, showing time 32 minutes Sponsored in 1960 by the Mental Health Film Board, New York Procurable on purchase from International Film Bureau, Inc , 57 E Jackson Blvd , Chicago 4, and on loan from state health departments

This film shows how one community organized, through the cooperation of both lay and professional citizens, to survey its mental health needs and establish a mental health center to meet them The film shows examples of the kind of preventive services a center might provide, but, most important, it shows the process by which a typical community might build a center This is an excellent film and is particularly well done in the sense that it portrays the kind of staff that such a community mental health center should have (i e , its over-all direction is by a qualified psychiatrist, with a psychologist and social worker under his direction) The photography is very good, and the narration is clear This is an excellent film for lay audiences and, particularly, for those groups considering the establishment of such a clinic It would also be useful for physicians speaking before such a group as an example of how to establish this type of clinic

DANGERS OF FIRST-PERSON NARRATION

It is always dangerous to write from the point of I' The reader is unconsciously taught to feel that the writer is glorifying himself, and rebels against the self-praise Or otherwise the I is pretentiously humble, and offends from exactly the other point of view In telling a tale it is, I think, always well to sink the personal pronoun The old way, Once upon a time," with slight modifications is the best way of telling a story —M Sadleir, Trollope A Commentary, New York, Farrar, Straus and Company, 1947, chap 9, page 283

BOOK REVIEWS

Diabetes, with a Chapter on Hypoglycemia By 54 authors Edited by Robert H Williams, M D, Executive Officer and Professor of Medicine, University of Washington, Seattle Cloth $20 Pp 793, with 192 illustrations Paul B Hoeber, Inc, medical division of Harper & Brothers, 49 E 33rd St, New York 16, 1960

Most likely it is inevitable, but somewhat amazing, nevertheless, that 774 pages can be devoted to a discussion of diabetes mellitus This fact alone is an indication of the fabulous accumulation of information on a disease that justifiably has been listed in the controllable category for almost 40 years Since the discoveries of Macleod, Collip, Banting, and Best, many milestones have been passed These include the preparation of crystalline insulin by Abel, the relation of the hypophysis to the pancreas by Houssay, the physiological function of glucagon by Murlin and Burger, the use of alloxan as a diabetogenic substance by Jacobs, and the clinical observation of Janbon on the hypoglycemic action of sulfonamides These items are examples only of the multifaceted subject Most of these investigators are still active in the laboratory Best and Houssay have contributed chapters to Williams' book

It would be folly to include a sentence or two of comment on each of the 48 chapters The clear and concise evaluation of carbohydrate metabolism by DeWitt Stetten Jr and Glenn E Mortimere is anticipated Stetten has an unusual faculty for lucid presentation of highly complex chemical information Although the precise action of insulin remains to be determined, Levine and Goldstein support the thesis that this substance acts by increasing the transfer of glucose across the cell wall Stadie, now deceased, has examined the evidence concerning the effects of insulin in relation to phosphates, the co-A-enzymes, and the oxidation of fatty acids

The clinical aspects of the disease are covered as extensively as is the discussion of basic chemistry and physiology The indications for the use of the oral diabetics are suggested by Williams Conservative conclusions are expressed I was particularly impressed with Ricketts' presentation of cardiovascular disease in diabetes, Kark and Gellman's presentation of renal disease, Fitzpatrick's discussion of dermatology, and Plum's discussion of neurologic complications This is an excellent volume, and I recommend it highly The editor is to be congratulated upon the selection of his contributors His capacity for persuading so many outstanding investigators to cooperate is remarkable

I have been particularly interested in the use of color figures in current medical literature There are 23 illustrations in full color in the monograph Several of these are excellent, others are only fair There is great need for improvement and uniformity of color reproduction in medical literature

JOHN H TALBOTT, M D

Some Papers on the Cerebral Cortex Translated from French and German by Gerhardt von Bonin, Professor of Anatomy, College of Medicine, University of Illinois, Chicago Publication number 332, American Lecture Series, monograph in Bannerstone Division of American Lectures in Classics in Science and Medicine Edited by Wiktor W Nowinski, Ph D, Dr Phil Nat, Associate Professor of Biochemistry, Director of Tissue Metabolism Research Laboratory, University of Texas—Medical Branch, Galveston, Texas Cloth $11 50 Pp 396, with 42 illustrations Charles C Thomas, Publisher, 301-327 E Lawrence Ave, Springfield, Ill, Blackwell Scientific Publications, Ltd, 24-25 Broad St, Oxford, England, Ryerson Press, 299 Queen St, W, Toronto 2B, Canada, 1960

With the transition from the anatomic to the physiological era in the investigation of the brain, it seemed appropriate to von Bonin to cull from history some of the outstanding contributions concerning the cerebral cortex as a basis for the appreciation of more modern concepts The problem of choice was prodigious, but the selections are judicious and of historical importance In translation there are now made available the studies of Flourens, the structure of the cerebral cortex by Baillarger, Broca's report on aphemia and the seat of the faculty of articulate language, the research of Fritsche and Hitzig on the electrical excitability of the cortex, and the studies of the functions of the cerebral hemispheres by Munk and Meyner There are also reports by Brodmann on comparative localization in the cerebral cortex, by von Monakow on localization of brain functions, and by Cajal on anatomic and physiological features of the brain The important research by Leyton and Sherrington on the excitable cortex of higher apes is the only article included that was originally written in English

The volume makes available in English a sampling of the works of some of the world's greatest investigators The translation is usually too literal and frequently awkward It is interesting to compare the methods of presentation of some of the old masters Those of Leyton and Sherrington and of Cajal are models of logical recording and of development of ideas Others are so rambling and disconnected as to make one wonder whether in style they could pass the watchful eye of a modern editor The book is recommended as a useful addition to the library of all those working in the broad field of neurology

BERNARD J ALPERS, M D

The Clinical Application of Antibiotics Volume IV Erythromycin and Other Antibiotics By M E Florey, M D Cloth $19 50, 84 shillings Pp 303, with illustrations Oxford University Press, Amen House, Warwick Sq , London, E C 4, England 417 Fifth Ave , New York 16, Amen House, 480 University Ave , Toronto 2 Canada, 1960

Shortly after World War II, a number of workers at Oxford who had been among the major contributors to the development of antibiotics and, particularly, to the production and application of penicillin proposed “to produce a book covering all aspects of their discovery, isolation and chemical, bacteriological and pharmacological characteristics as well as their clinical use, where this has been found possible’ The rapidly accelerating pace at which work in this field was moving and the tremendous growth of the literature that accompanied the resulting developments made this impossible However, in 1949, seven of these Oxford workers (headed by Sir Howard W Florey) succeeded in getting out two volumes entitled “Antibiotics which dealt mainly with the history and developments in the laboratory These volumes comprised 1,774 pages and contained about 3,500 bibliographic references The clinical applications were to be covered in a third volume to be authored by Lady Mary E Florey, the only clinician among the original seven contributors This, too, proved to be a much greater task than was originally contemplated, and it soon became clear that the originally planned third volume would have to be expanded into further ones The original third volume appeared in 1952, it was entitled “The Clinical Applications of Antibiotics (Penicillin) and dealt primarily with the many clinical uses of that antibiotic, including only a brief account of relevant laboratory developments At that time, another volume dealing with the clinical applications of other antibiotics was planned Since then, two such additional volumes have been completed One of them, volume 3, under the same general title, was finished in 1956 and published in 1957 Its subtitle was ‘ Chloramphenicol and the Tetracyclines, and it comprised 393 pages and nearly 1,700 references In volume 2, which has not yet appeared, the author proposes to deal with the antibiotics applicable to the treatment of tuberculosis

Volume 4, the last of the series, was completed early in 1959 and covers other antibiotics The first chapter deals with erythromycin and a number of antibiotics related to it by reason of cross-resistance, the second considers those whose major activity is against the staphylococcus and other gram-positive organisms Other chapters deal with antibiotics directed against various organisms including gram-negative bacteria, those with limited application because of toxicity, and a miscellaneous group directed against protozoa fungi and neoplastic cells The most important part of this volume, however, is the long last chapter on the choice of an antibiotic This subject is dealt with first in a general way, then specifically with respect to disease due to individual pathogens, and finally with regard to diseases affecting various systems This may well be the most valuable reference source to the practicing clinician as it brings together the basic observations and clinical effects and presents the practical aspects of their application

Lady Florey is to be congratulated on her courage, diligence, and perseverance which have resulted in a great and useful contribution The Oxford University Press deserves our gratitude for undertaking the task of publishing this large work and for the superior quality of the product The high price which will probably amount to more than $75 for the four volumes may limit the distribution of these to libraries and a few specialists with funds for the purchase of such volumes, but this price is undoubtedly justified by current costs of production

MAXWELL FINLAND, M D

Detoxication Mechanisms The Metabolism and Detoxication of Drugs, Toxic Substances and Other Organic Compounds By R Tecwyn Williams, Ph D , D Sc , Professor of Biochemistry in University of London at St Mary s Hospital Medical School, London Second edition Cloth $19 Pp 796 John Wiley & Sons, Inc , 440 Fourth Ave , New York 16, 1959

This is the second edition of a widely accepted textbook devoted to a review of the metabolism and detoxification of drugs, toxic substances, and other organic compounds The rapid increase in our knowledge of the fate of chemical agents in animal organisms is reflected in the increased size of this revised text The marked increase in the use of synthetic organic chemicals in all spheres of human activity has produced a concomitant increase in the biologic knowledge of organic compounds foreign to the human body In the postwar years, knowledge has been acquired about some aspect of the metabolism of most major groups of synthetic organic chemicals However, the large number of organic chemical compounds now available (approximately 600,000) offers an unlimited field of research on the effects of these agents on plant and animal metabolism

The introductory chapter is devoted to general remarks about biochemical reactions of synthetic organic compounds and to a short review of the history of detoxicating mechanisms The remaining chapters are devoted to the metabolism of the major categories of organic chemical agents The concluding chapter is devoted to several hypotheses related to the metabolism of foreign compounds and their detoxificating mechanisms Attention is drawn to certain so-called biologically inert compounds which apparently undergo little or no change in the tissues and are often excreted unchanged in the urine and feces Specific differences in the rate of metabolism of drugs are discussed, and the reactions of man as compared with those of experimental animals are tabulated for 11 representative organic medicinal agents References to significant current literature accompany each chapter, and an extensive subject and author index is provided

This text should be a valuable if not indispensable reference work for all those desiring an understanding of the pharmacology and toxicology of drugs, pesticides, food additives, and industrial chemical compounds

Bernard E Conley, Ph D

Leukocyte Antigens and Antibodies By Roy L Walford, M D, Assistant Professor of Pathology, University of California School of Medicine, Los Angeles Cloth $6 75 Pp 182, with 7 illustrations Grune & Stratton, Inc, 381 Park Ave S, New York 16, 15/16 Queen St, Mayfair, London, W 1, England, 1960

The number of diseases in the pathogenesis of which an antigen-antibody reaction is involved is constantly rising The role of this immunologic reaction in the cause of diseases of erythrocytes is well established, and so is its application to diagnosis, treatment, and follow-up Similar reactions have been demonstrated in some of the lesions affecting leukocytes However, the methodology of testing, the reproducibility of the tests, and interpretation of the results are still not well established The author himself has made valuable contributions to the subject In the first chapter, the various techniques, their respective advantages and disadvantages, and the sources of error are reviewed The remainder is a discussion of current knowledge as it relates to the following questions 1 Are there blood groups in leukocytes? The answer seems to be affirmative as it applies to the AB factors but not to the other blood factors 2 Are leuko-agglutinins iso-antibodies or auto-antibodies? Most observed instances, especially those linked to transfusion reactions are of the former variety, auto-agglutinins are less frequent 3 What is the role of leuko-agglutinins in allergic neutropenia? 4 Are leukocytic antigens and antibodies involved in the L E phenomenon? We have learned a great deal about this interesting reaction since it was reported by Hargraves in 1948 With very few published exceptions, the test has been found highly specific for lupus erythematosus and closely related disorders, although it is neither species nor tissue specific 5 What role do leukocyte agglutinins play in immunity reactions involved in tissue transplantation? Injection of leukocytes into mature animals may lead to transplantation immunity, and a similar injection into the newborn may produce tolerance to later tissue transplants 6 In what clinical conditions are leukocyte antibodies found?

These are only a few of the many questions which modern research has been trying to solve with varying degrees of success The author has done an excellent job condensing a difficult subject lucidly in a minimum of space There is an extensive bibliography

Israel Davidsohn, M D

The Art of Lecturing By G Kitson Clark, Litt D, and E Bidder Clark, O B E 3s 6 d Pp 41 W Heffer & Sons, Ltd, 3-4 Petty Curry, Cambridge, England, 1959

At least part of the low rating of lectures in the curriculum stems more from the poor quality of the speaker than from any inherent fault in lectures qua lectures Although there are many treatises, manuals, and texts on techniques of lecturing, from my experience in listening to people present scientific material at medical meetings I suspect that most speakers are oblivious to them While one probably can do well enough by taking as his model any good speaker, it is well to remember a few simple rules and regulations which a good speaker needs to keep in mind regardless of his experience Very few speakers are without a few minor and characteristic tics Some interrupt every sentence by uhs, ohs, ahs, or grimaces Others fail to address the platform, talk into their vest, wave the flashlight pointer around as though they were in competition with a planetarium, indicate that they spent no time on practice or rehearsal, or present charts and slides which are so pitiful as to insult the audience and give a sad commentary on the speaker's intelligence While this little book by the Clarks will not make a good speaker out of a bad one, at least it gives a good clear reading of the map, pointing out head winds, wire, land mines, and booby traps, avoidance of which would make any physician or any medical teacher do a better job when he lectures

William B Bean, M D

From the A M A *Archives of Internal Medicine* **105** 818 (May) 1960

Pediatric Anesthesiology By M Digby Leigh, M D, *Associate Professor of Surgery* (Anesthesia), University of Southern California, Los Angeles, and M Kathleen Belton, M D, Assistant *Professor of Surgery* (Anesthesia), University of Southern California In collaboration with George B Lewis, Jr, M D, and Edward *B* Scott, *M D*, *Assistant Attending* Anesthesiologist, *Childrens Hospital of* Los Angeles [First edition known as Pediatric Anesthesia] *Second* edition Cloth $12 Pp 461, with 203 illustrations The Macmillan Company, 60 Fifth Ave, New York 11, *Brett-Macmillan* Ltd, 132 Water St, *S*, Galt, Ontario, Canada, 1960

This second edition has been anticipated for some time and more than lives up to our high expectations It is an entirely new book in plan and content and denotes the great expansion undergone in the practice of pediatric anesthetization since 1948

The first section, devoted to evaluation of the patient, is not an exhaustive description of the preoperative examination, as the title might suggest, but a compendium of pediatric information of all sorts that might have bearing on infants and children coming to operation Among a host of topics we find a description of the Klipple-Feil syndrome, a practical explanation of acid-base disturbances, anatomy of cardiac defects (with catheterization data), and a resume of pulmonary physiology

The second section is a clear, concise description of anesthetic agents, techniques, and equipment Although all methods and agents are fairly evaluated, the authors appear to favor nonrebreathing and circle absorption techniques, with endotracheal intubation Cyclopropane and halothane are suggested most frequently, although emphasis is appropriately placed on painstaking patient care rather than the choice of agent The third section briefly presents a basic form of preoperative preparation of patients Sedation follows the traditional plan of administration of barbiturate, narcotic, and antihistaminic, and there is complete and refreshing disregard for the entire field of tranquilizing agents

In the fourth section, devoted to the anesthetic management of surgical procedures, we have the real meat of the text, it represents the clinical experience of outstanding authorities and describes the treatment of every type of case The authors have provided us with ample illustrations, well-chosen references, and a tremendous amount of information in one volume

ROBERT M SMITH, M D

The Merck Index of Chemicals and Drugs An Encyclopedia for Chemists, Pharmacists, Physicians, and Members of Allied Professions Paul G Stecher, editor Chemical Monographs M J Finkel, M D Medical Uses O H Siegmund, D V M Veterinary Uses B M Szafranski, assistant editor Seventh edition Cloth $12 Pp 1641 Merck & Company, Inc, Rahway, N J 1960

After eight years this excellent reference book has appeared in its seventh edition It serves as a single-volume encyclopedia of over 10,000 chemical entities for use by physicians, pharmacists, chemists, and members of other allied professions It contains a cross-index of over 30,000 names Over 3,400 structural formulas are included Several sections among the many of interest to physicians are the cross-index of names, and those concerning radioactive isotopes used in medical therapy and diagnosis, first aid in poisoning, calories in foods, some biological units and their use, prescription notation, metric and U S systems of weights and measures, conversion formulas, and isotonic solutions For each chemical entity, certain physical data are given along with a description of commercial use, information on medical use, brief statements on dosage, toxicity, and contraindications Pertinent references are often included This is a helpful reference book with which physicians might become acquainted as a ready source of concise technical information

WALTER WOLMAN, Ph D

Anatomy A Regional Study of Human Structure By Ernest Gardner, M D, Donald J Gray, Ph D, and Ronan O Rahilly, M Sc, M D Cloth $15 Pp 999, with illustrations by Caspar Henselmann W B Saunders Company, 218 W Washington Sq, Philadelphia 5, 7 Grape St, Shaftesbury Ave, London, W C 2, England, 1960

It is a pleasure to note the appearance of a textbook of anatomy written in readily understandable language which has made a real contribution toward the correlation of the basic sciences of physiology, pharmacology, and embryology along with the study of growth anatomy The authors have succeeded in presenting a text that is unusually concise and succinct These features are wonderfully complemented by the great numbers of well-prepared illustrations, plates, and tables, most of which are new and not merely reproductions of previously utilized figures

This enlightening text has apparently bypassed a great deal of the minutia that so frequently burdened the text of previous anatomic works and has substituted a great wealth of correlative material in the form of many significant radiographs as well as a host of well-prepared diagrammatic sketches There is relatively little new in anatomy, and all that can be expected of a textbook of this discipline is the presentation of the matter in a simple, straightforward fashion that is easy to comprehend and well illustrated This book fulfills these requirements and is highly recommended for use by students of medicine, dentistry, and other related fields It should also provide a refreshing and enlightening review of the subject for those engaged in the various health professions

JOHN L TERRY, M D

Patterns of Professional Education By William J McGlothlin Vice-President, University of Louisville, Louisville, Ky Cloth $6 75 Pp 288 G P Putnam s Sons 210 Madison Ave, New York 16, 1960

In the present climate of critical reappraisal of education in the United States, a currently accurate and objective comparison of education for the various professions could well provide useful information for members and educators of each profession This book represents such an attempt It presents a comparative study of architecture, business administration, engineering law, medicine, nursing, psychology, social work, teacher education, and veterinary medicine The book is organized to compare the 10 fields in terms of the aims and objectives of curriculum, methods of instruction, faculty, recruitment and selection of students, relations between the professional school and the university, accrediting, and instruction in professional ethics A total of 354 references are listed, only 184 of which are cited in the text None refer to previous publications by the author

The book contains a prosaic presentation of cursory information about the 10 fields largely without value judgments and with analysis and synthesis confined for the most part to the brief concluding chapter Although there is a necessary lag between completion of a manuscript and book publication, the delay in this instance appears to be unusually great Of the 184 references cited in the text, only five are as recent as 1958, none of these relates to medicine At least in medical education, and probably in the other fields as well, the information presented is not based on relatively current references but rather on publications of 5 to 10 years ago Much that was factually correct then in medical education no longer represents current policies, viewpoints, concerns, or activities This is probably the case in the other professions as well

GLEN R SHEPHERD, M D

Recent Advances in Surgery Edited by Selwyn Taylor, D M, M Ch, F R C S, Surgeon, King's College Hospital, London Foreword by Sir James Paterson Ross, K C V O, M S, President of Royal College of Surgeons Fifth edition Cloth $13 Pp 500, with 160 illustrations Little, Brown & Company, 34 Beacon St, Boston 6, J & A Churchill, Ltd, 104 Gloucester Pl, Portman Sq, London, W 1, England, 1959

All aspects of surgery and the surgical specialties are not reviewed exhaustively by the 28 contributors to this new edition, but selected subjects considered to be of current interest have been chosen for discussion These may be grouped as cardiac and vascular surgery, pulmonary surgery, problem of cross-infection, transplantation of tissues and organs, lymphatic system, body fluids, artificial kidney selected urologic topics, hydrocephalus, parotid gland, and surgery of the gastrointestinal tract including discussions of argentaffinoma, portal hypertension, cancer of the breast and the endocrine glands Each author has succinctly presented the current concepts of his subject, giving enough detail and sufficient bibliographic references so that the reader may fully understand the problems under consideration

In some fields an extensive experience has been gained so rapidly that it is now possible to present concrete opinions on subjects which were considered experimental surgery when the fourth edition was published This is particularly well exemplified in the section on cardiac and vascular surgery where there has been rapid development of new techniques as well as extensive investigation into physiological problems concerning arterial blood flow and extracorporeal circulation Except in these fields, however, advances have been primarily in the realm of studies of physiological alterations rather than operative techniques There has always been a close relationship between advances in surgery and advances in the basic sciences, but, today, this relationship is closer than ever before One subject that emphasizes this fact is tissue transplantation The primary advances are being made in the fields of biochemistry, immunology, and genetics, and the ultimate solution of the problems involved in tissue transplantation will be predicated on an understanding and a correlation of information gained from investigations in these areas

This volume is highly recommended as a ready reference source for review of the new ideas and changing patterns of therapy in the practice of surgery

GEORGE L JORDAN JR, M D

The Hæmolytic Anæmias Congenital and Acquired Part I The Congenital Anæmias By J V Dacie, M D, F R C P, Professor of Hæmatology, University of London, London Second edition Cloth $7 Pp 339, with 118 illustrations Grune & Stratton, Inc, 381 Park Ave S, New York 16, 15/16 Queen St, Mayfair, London, W C 2, England, 1960

The first edition of Dr Dacie's book was recognized by hematologists as the most authoritative and comprehensive treatment of the hemolytic anemias This new edition should be most welcome for the advances in the area of hemolytic diseases since the first edition appeared in 1954 have been numerous The second edition will be divided into two volumes Only volume 1 is published at this time Volume 2, when completed, will deal with acquired and secondary hemolytic anemias, drug-induced hemolytic anemias, paroxysmal nocturnal hemoglobinuria, and hemolytic disease of the newborn

Volume 1 is devoted to a presentation of the hereditary hemolytic anemias The subjects discussed include general features of increased hemolysis hereditary spherocytosis, hereditary elliptocytosis, hereditary nonspherocytic hemolytic anemia, "erythropoietic porphyria," congenital Heinz-body anemia, Mediterranean anemia (thalassemia), and hereditary hemoglobinopathies

The book is well organized and clearly written Newer information on the fine structure of the normal and abnormal hemoglobins is unfortunately mentioned only briefly and superficially This shortcoming does not in any way detract from the excellent morphologic and clinical descriptions No hematologist can afford to be without this volume, it has no equal

GEORGE E CARTWRIGHT, M D

QUESTIONS AND ANSWERS

POSTOPERATIVE HYPOTHYROIDISM

To the Editor —*A 33-year-old woman with a possible endocrine deficiency had a subtotal thyroidectomy in 1956 because of a classic thyrotoxicosis and since then she has been more or less hoarse and has had a deep masculine voice At the time of the operation the recurrent laryngeal nerves were apparently not injured in any way In 1958 she began to notice vaginal spotting between periods Her periods have been irregular and more frequent than normal, but in general she has felt relatively well A dilation and curettage performed in 1958 revealed hyperplasia of her endometrium*

She was fairly well after this procedure, but the abnormal bleeding has recurred Various hormones given in an attempt to restore a normal menstrual cycle have been of little help Repeated cervical smears have shown no abnormal cells, and physical examination fails to reveal any defect of the pelvic organs There is no hirsutism, her secondary sex characteristics appear to be normal, and her libido appears to be unchanged A laryngologist reported some thickening of the vocal cords but in general good function At present the patient is taking 120 mg of thyroid extract daily and a dextroamphetamine sulfate derivative for weight reduction Is there any type of glandular dysfunction that might explain her symptoms?

George R Farrell, M D , San Diego, Calif

Answer —This patient exhibits many of the sequelae of secondary hypothyroidism Dysfunctional bleeding can be associated with myxedema The deep voice changes are in keeping with vocal cord thickening which was observed by the examining laryngologist The correspondent mentions that the patient is currently taking 120 mg of desiccated thyroid, but the length of time that the patient has been receiving this is not mentioned It usually takes 8 to 12 weeks of the optimum therapeutic dose to effect improvement If, after such a period, the patient is not improved, a larger dosage may be indicated In addition to the basal metabolism rate, serial cholesterol determinations may be helpful in following the patient's response to the administered thyroid It would be well to inquire from the patient whether she has been faithful in taking the prescribed medicament

CHRONIC CHOREA

To the Editor —*A 24-year-old woman has inquired about the probability of her having chronic chorea and of transmitting it to her children The questioner's mother, now aged 62 years, was given a diagnosis of chorea 10 years ago, on the basis of choreiform movements with mental deterioration in adult life All blood relatives are known for four generations prior to the affected person, and none had any form of degeneration of the central nervous system, and, with one or two exceptions, all lived out the average span of life Are there known instances of chronic chorea arising in a family without antecedent instances and then being transmitted? What are the chances of the questioner's children having this disease?*

Stuart H Lewis, M D , Wayne, Pa

Answer —On rare occasions we find a pedigree of chronic chorea in which the first affected person had definitely normal parents who lived to old age In these cases it is entirely reasonable to assume that a mutation for chronic chorea has occurred in the gametes of one or the other of the normal parents Over long periods, the families with chronic chorea tend to die out, and the fact that the disease is still with us means that every now and then there is a new mutation from the normal gene to that for this disease, and that the descendants of this new mutation replace those families in which the gene has died out

This young woman has a 50% chance of having the dominant gene for chronic chorea and of developing the disease in due course If she does have the unwanted gene, each of her children also has a 50% chance of having the gene and later developing the disease If she does not have the gene, she will never have the disease and none of her descendants is likely to have it One must hope that the young woman failed to inherit the gene for chronic chorea, there is an even chance that this was the case

HEMOSPERMIA

To the Editor —*What is the cause of asymptomatic bloody semen?*

Dan Jordan, M D , Bethel, N C

Answer —Asymptomatic hemospermia, or the finding of blood in the semen, is not unusual It is usually caused by a seminal vesiculitis or a chronic passive congestion in the seminal vesicle The bleeding probably occurs secondary to rupture of small vessels in the seminal vesicle In some patients

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The answers here published have been prepared by competent authorities They do not however represent the opinions of any medical or other organization unless specifically so stated in the reply Anonymous communications cannot be answered Every letter must contain the writer's name and address but these will be omitted on request

the seminal vesiculitis is due to bacterial infection and is secondary to prostatitis which can be demonstrated on prostatic smear More often the seminal vesiculitis seems to be abacterial in origin, and the cultures and examinations of the prostatic fluid do not reveal any specific organisms Occasionally a case of hemospermia may be due to carcinoma of the seminal vesicle, or, in rare instances, to inflammatory or neoplastic lesions of the prostatic urethra or verumontanum These instances, however, are usually accompanied by severe symptoms indicating that the disease is localized in the region of the prostate or prostatic urethra

The typical case of asymptomatic hemospermia is that of the finding of blood in the semen without any indication that difficulty exists This is often recurrent, and some patients have recurrent attacks of blood in the semen over many years, usually subsiding without any specific treatment It is important to rule out by palpation, and, if necessary, by cystoscopy and x-ray studies, the presence of a neoplasm in the region of the seminal vesicle It is also important not to overtreat these patients We usually resort to gentle massage of the prostate and seminal vesicles and reassurance of the patient with chemotherapy, as indicated by the bacteriological findings of the prostatic fluid Instrumentation is avoided, with the exception of cystoscopy, in many cases on the initial visit, to rule out any neoplasm Reassurance is as important as anything in the therapy It has been suggested that estrogens may reduce the incidence of bleeding, but we have not had any particular success with this method and are reluctant to give estrogens to sexually active men

BRUCELLOSIS

To THE EDITOR —*A veterinarian inadvertently inoculated himself with* Brucella *strain 19 while vaccinating cattle A mild local reaction with adenitis, generalized myalgia, malaise, anorexia, weakness, and fever promptly developed, the symptoms have responded slowly to treatment with streptomycin, tetracycline rest, and a sulfonamide On the day of his accident the patient felt the beginnings of symptoms of recurrence of his chronic brucellosis Is the above strain pathogenic to human beings? Is any other treatment, local or systemic, indicated?*

Fred B Ely, M D , Orland, Calif

ANSWER —It has been demonstrated many times in the past that *Brucella* strain 19 will produce disease in man This usually occurs when persons inadvertently inoculate themselves with the organism Several cases are reported every year, usually among veterinarians, their assistants, and livestock handlers Vaccination with strain 19 frequently produces an exacerbation in persons who have previously had brucellosis This is especially true among veterinarians and farmers Russian investigators claim that a variant of strain 19 is being used successfully in immunizing human beings According to a recent report, they have vaccinated 2,500,000 persons with the strain 19 variant They admit that it occasionally causes severe reactions

ANSWER —*Brucella abortus,* strain 19, does on rare occasions cause human infection (Spink, *Ann Int Med* 47 861 [Nov] 1957) All the reported cases have been in persons who have accidentally inoculated themselves while vaccinating cattle Two types of clinical illness have been observed In the case of a veterinarian, if a previous *brucella* infection has occurred, localized and systemic manifestations appear within a few hours after accidental inoculation This is due to acquired *Brucella* hypersensitivity, but, if a person has not had a previous infection, there may be a delay of several days before a generalized illness occurs Under these circumstances, localized manifestations may not appear The treatment in all instances is the administration of a tetracycline in an oral dose of 0 5 Gm three or four times a day for 10 to 14 days It is probably not necessary to use either streptomycin or a sulfonamide

CORONARY OCCLUSION IN HEMOPHILIACS

To THE EDITOR —*Is there any record of hemophiliacs having suffered from coronary occlusions? This would be of interest to a physician treating these patients with anticoagulants*

Theodor Friedrichs, M D
Astoria, Long Island, N Y

ANSWER —There is little published literature regarding arteriosclerosis and myocardial infarction in hemophiliacs In 1954 Brovin (*Arch mal coeur* 47 351 [April] 1954) reported a case of myocardial infarction in a patient with mild hemophilia Three years later, Stewart and Acheson (*Lancet* 1 1121 [June 1] 1957) documented a case of widespread atherosclerosis involving the coronary arteries in a hemophiliac, and more recently Borchgrevink (*Lancet* 2.1229 [June 13] 1959) also reported posterior wall myocardial infarction in a hemophiliac with a history of angina pectoris of 10 years' duration Routine anticoagulant therapy in the first few days was discontinued as soon as the hemorrhagic diathesis was diagnosed, although there had been a history of abnormal hemorrhagic phenomena of rather mild degree, beginning at the age of 25 years This patient showed 16% of normal concentration of factor VIII (antihemophilic factor) in his plasma Six male relatives also had hemophilia, with levels of antihemophilic factor varying from 12 to 17% These data, together with the clinical history, reflect the mildness of his derangement

Study of such cases may shed light on the pathogenesis of atherosclerosis According to the Rokitansky-Duguid-Astrup concept, imbalance between procoagulant and anticoagulant forces in vivo may induce fibrin deposition on vessel walls, in this way initiating the pathological sequence associated with arteriosclerosis If arteriosclerosis can be demonstrated to be exceedingly rare in hemophiliacs, or for that matter in other heredofamilial hemorrhagic disorders associated with profound clotting defects, this would tend to support the theory This has been discussed recently by Astrup (*Lancet* 2 745 [Oct 12] 1957), where one can also find speculation by Borchgrevink regarding the rationale for anticoagulant therapy based on similar thoughts

PROTEIN BOUND IODINE TEST

To THE EDITOR —*On inquiry I have been given two answers regarding the protein bound iodine (PBI) test made while the patient is taking thyroid substances Both authorities agreed that while liothyronine is taken, the PBI value is depressed There was, however, disagreement about the results of the test while exsiccated thyroid is being taken Can the PBI test be used to measure the therapeutic effect of this medication in hypothyroidism?*

F C Katzenstein, M D , Salem, Ill

ANSWER —The PBI is usually a reliable index of the adequacy of desiccated thyroid therapy in hypothyroidism, but the PBI test, like all laboratory tests, is occasionally subject to analytical errors which produce inaccurate results In addition, there is the occasional patient receiving adequate doses of desiccated thyroid whose PBI value remains below 3 0 mcg %, in spite of the complete absence of clinical symptoms or signs of myxedema Increasing the dose of desiccated thyroid in such patients serves only to produce tachycardia, nervousness, shaking, and increased warmth Rigid reliance on the PBI test in this situation is not justified The final decision concerning the adequacy of desiccated thyroid therapy rests with the clinician The average daily requirement of desiccated thyroid for correction of myxedema is 90 mg , although large persons may require as much as 120 and, rarely, 180 mg With these doses, the PBI is usually in the normal range of 3 0 to 8 0 mcg %

VASCULAR ACCIDENTS

To THE EDITOR —*Are vascular accidents more likely to occur after exercise at altitudes of 10,000 to 11,000 feet than at sea level?*

Dwight C Sigworth, M D , Long Beach, Calif

ANSWER —The precipitating causes for vascular accidents are not known with certainty There is much argument about the effect of exercise, though there is wide belief that severe exercise may precipitate a myocardial infarct in a person with serious coronary artery disease Even the most careful statistical studies have not answered this question As with many clinical problems, it must remain in the realm of probability rather than established fact Of the possible varieties of vascular accidents, such as hemorrhage, thrombosis, and embolism, there is no body of controlled evidence comparing their occurrence at sea level and at high altitudes If all other factors were kept constant, there would probably be some increase in the likelihood of such accidents at high altitudes because of the fact that exercise at such altitudes has a greatly increased cardiorespiratory cost from hypoxia In rare vascular accidents, such as rupture of the aortic valve, rupture of the aorta, rupture of an aneurysm, or the initiation of a dissecting aneurysm, a better case can be made out for the precipitating role of exercise at high altitudes In every case the effect of altitude would depend on many factors other than exercise, particularly the subject s physique, degree of training, fitness, state of general health, and the existence and extent of underlying vascular disease

INCONTINENCE OF URINE

To THE EDITOR —*Is there anything new that is of value in treating incontinence of urine in the male? I have tried such measures as the Birmingham clamp, and the Davol apparatus but have not found them satisfactory Operation is contraindicated, since the patient concerned is 82 years of age and inoperable He still has a slight enlargement of the prostate, notwithstanding two previous transurethral resections He has an asymptomatic left kidney calculus and multiple calculi in the remaining portion of the prostate His bladder is contracted (with a capacity of 60 cc), and he is obliged to urinate six to seven times during the night There is no incontinence during the night, but it is troublesome during the day*

M D , California

ANSWER —The fact that this patient has incontinence only during the day means that he still has some effective sphincter control, but not enough to hold back the urine when he is in the upright position His low bladder capacity probably precludes the use of an indwelling urethral Foley catheter In spite of the fact that the patient is considered to be inoperable, experience shows that many such patients can tolerate a permanent suprapubic mushroom catheter, placed by means of a suprapubic cystostomy performed under local anesthesia, and maintained for long periods, without changing, by daily irrigations with an anticalcium deposit solution, such as Renacidin, in conjunction with daily irrigations with a 1 10,000 solution of potassium permanganate It is surprising how well some of these patients react to this treatment

PERIPHERAL NEURITIS

To the Editor —*A 56-year-old man, under treatment since early January for mild diabetes controlled by 1 Gm of tolbutamide daily and diet, developed marked weakness of the foot flexors of the right leg about one month ago The paresis was abrupt in onset The patient had followed exactly a 1,300 calorie diet and had lost 55 lb (74 9 kg) in 16 weeks No vitamin supplement was used At times he has mild numbness and tingling in the right leg and foot, but no sensory changes were found Pulsations are normal He has used no other drugs Does this brief history contain any etiological clues? What tests might prove of value? Should any supportive therapy be instituted now?*

M D, Iowa

Answer —The brief history as given indicates a peripheral nerve involvement in the right leg The description of the weakness does not enable one to differentiate between a peroneal or tibial nerve lesion One might conclude that both or the lower portion of the sciatic nerve are involved Diabetic neuropathy may develop even in a patient with mild diabetes, and this is probably the basic etiological factor in the present case The pathogenesis of diabetic neuropathy is not clear, but in this type of an apparently mononeuritic lesion, involvement of the vasa nervorum is considered to be present Electromyography and nerve conduction velocity studies would be helpful in delineating the extent and intensity of the neural disorder It probably would be worthwhile to obtain roentgenograms of the lumbosacral spine and to perform a lumbar puncture, including manometric tests, to rule out an intraspinal or root lesion Supportive physical therapy with the involved muscles should be instituted to help maintain their integrity

ANTICOAGULANTS AND DIABETICS

To the Editor —*Long term anticoagulant therapy after coronary infarct is well accepted The lipotropic effect of heparin has been noted These conclusions have suggested that a diabetic who has had a coronary infarct be treated with a daily prophylactic injection of heparin A cardiologist at a recent meeting suggested this therapy I am interested in further opinions and the recommended dosage*

Milton C F Semoff, M D, Tucson, Ariz

Answer —The status of the proposed heparin treatment for a diabetic patient who has had a myocardial infarct is a matter in which varying opinions have been expressed Heparin has been given by injection, particularly in patients who have an elevated serum level of cholesterol, and other lipids have been given in an attempt to reduce the lipemia, while at the same time affecting favorably angina pectoris and coronary sclerosis The results in such series were equivocal A similar attempt in diabetic patients to relieve the pain of intermittent claudication by the use of depot heparin was not successful Certain hazards exist in the use of daily heparin injections The patient must be under continuous observation with frequent determinations of the prothrombin time In some diabetic patients, a severe hemorrhage has occurred after very small doses of anticoagulant Although the use of heparin will lower the level of lipids in the blood, the basic lesion in the arterial wall would hardly be affected The question is still a matter for further research

ARTHRITIC PAIN

To the Editor —*A 62-year-old man has had arthritic pain in his arms and legs for the past 10 years These were so severe that it was difficult for him to get out of bed or rise from a chair and, when he went out, it was a while before he felt relieved enough to go to work He received a puncture wound in his palm, for which I gave him an injection of tetanus antitoxin Since then he has had no more pain and rises from bed and chair without discomfort What can be the cause of this sudden change?*

Samuel S Schept M D, North Bergen, N J

Answer —It would appear that the patient experienced a nonspecific foreign protein reaction from the antitoxin, with resultant amelioration of his rheumatic symptoms In times past typhoid vaccine given intravenously or sterile milk intramuscularly was commonly used to relieve the acute symptoms of rheumatoid arthritis and fibrositis Although less popular now than formerly, it is still used in some clinics and was mentioned in the last issue of the Primer on Arthritis and Rheumatic Diseases (*J A M A* 171 1205 [Oct 31] 1959)

ACTIVATED CHARCOAL

To the Editor —*How does activated charcoal differ from ordinary charcoal?*

F E Palmer, M D, Sterling, Colo

Answer —The *National Formulary* defines activated charcoal as "the residue from the destructive distillation of various organic materials, treated to increase its absorptive power " The *U S Dispensatory* (1955) contains a two page monograph on activated charcoal from which the following excerpt is taken

"Destructive distillation of organic matter tends to be molecularly disruptive, so that extensive development of surface occurs in the manufacture of charcoal but special treatment is required to activate the surface Such activation may be effected by treating the charcoal, at high temperature, with steam and carbon dioxide, air in small quantities may be admitted as a mild oxidant for certain contaminating substances Strong dehydrating substances, such as sulfuric or phosphoric acid, or zinc chloride, are also employed in preparing some activated charcoals, their action, presumably, is to break down or to assist in breaking down organic substances so that carbonization may be facilitated For many purposes, certainly when used medicinally, activated charcoals or carbons, as they are more often called, must be washed with acid and water to remove any inorganic matter that may be present'

A more comprehensive discussion of the various methods used in the preparation of activated charcoal may be found in Volume II of the Encyclopedia of Chemical Technology" (New York, The Interscience Encyclopedia, Inc, 1948)

BACTERIAL ANTIGEN

To the Editor —*Please send me information on use of acellular bacterial antigen complex (B A C) in the treatment of infections*

Melvin Marx Jr, M D, Clarksville, Texas

Answer —Bacterial antigen complex is prepared by a special method which combines the soluble specific substances obtained from bacteria with the respective toxins and enzymes produced by pathogens in vitro and in vivo The manufacturer recommends the use of single-strain preparations for skin tests If there is an immediate skin reaction and a favorable clinical response after skin tests, the appropriate preparation is selected for therapeutic administration In exceptionally severe cases, the preparation of an autogenous bacterial antigen complex is recommended The dosage schedule in patients with chronic respiratory conditions, such as infectious asthma, calls for intradermal injections at weekly intervals beginning with 0 02 ml and an increase in the dose by increments of 0 02 ml In acute conditions small intradermal injections are given every 72 hours Favorable results have been reported in studies by Shinefield (*New York J Med* 56 1466 [May 1] 1956) and Spielman (*ibid* 55 1603 [June 1] 1955)

NIGHTMARES

To the Editor —*Could you suggest the cause or cure for nightmares experienced by an elderly man? These are not connected with medicaments or other specific factors, as far as I can determine*

Ursula G Mandel, M D, Los Angeles, Calif

Answer —The most frequent cause in elderly patients of terrifying dreams, apparently causeless in character, relates to actual physical changes within the patient They are usually associated with alterations in blood circulation A sudden spasm of a blood vessel anywhere in the patient's body can result in sudden, brief pain that is interpreted by the patient with a dream response Thus, instead of awakening, the patient endeavors to prolong sleep by interpreting the pain of the spasm as a dream experience There is also the possibility of terrifying dreams relating to death fears, but these are usually intimately associated with many other symptoms Relief can often be afforded by simply reassuring the patient that he need not anticipate dire results, and that the terrifying dreams and spasm are 'aging pains, comparable to the so-called "growing pains" of youth

CHRONIC PAROTITIS

To the Editor —*After eating, a patient has swelling of both parotid glands, but can express saliva which is without purulent material by pressing on these glands As a rule, the condition exists in only one gland at a time, and occasionally is accompanied by a low-grade fever There is apparently no obstruction of Stensen's duct, but clinical examination seems to indicate that this condition affects the glandular portion itself This condition started in the left parotid gland and has been present for 10 years, but in the past year it has affected the right gland intermittently What is the probable diagnosis and the best treatment?*

Howard D Cogswell, M D, Tucson, Ariz

Answer —Apparently this patient has chronic bilateral parotitis, which often is due to alpha-hemolytic streptococci Antibiotics are of little, if any, value, but a vaccine prepared from material expressed from the parotid ducts often will cause the symptoms of this condition to disappear Such a vaccine must be administered weekly for several months

MUSCULAR CRAMPS

To the Editor —*What can be done for a 64-year-old woman who suffers severely with cramps in her feet and legs? Her general condition is excellent The cramps are worse after a trip, especially when she drives*

Roy A Douglass, M D, Huntingdon, Tenn

Answer —Rare causes for cramps in the feet and legs, such as hypocalcemia, hypopotassemia, and certain neurological disorders, should be excluded since specific therapy might be of value in these instances Usually, however, no cause is found for cramps in the feet and legs of elderly patients Treatment must be non-specific and, unfortunately, is all too often ineffective Suggestions for treatment include any or all of the following 0 2 or 0 4 Gm of quinine sulfate, every four to six hours, 25 or 50 mg of diphenhydramine hydrochloride three or four times a day, or 350 mg of carisoprodol three or four times a day

DRINKING WATER WITH MEALS

To the Editor —*Drinking water or other fluids with meals is strongly recommended by some physicians but considered optional by others What is the reason for prescribing fluids with food? What untoward results may follow if this dictum is ignored?*

M D, Ohio

Answer —The recommended allowance for water is about 2 5 liters a day In the average diet, a great part of this water comes from solid foods The habit of drinking water should be encouraged, since water is extremely important to the normal functioning of the body Water consumption at meal time is advised if the food is thoroughly masticated and if the water is not used to wash down the food Water is also thought to aid digestion by promoting the flow of digestive juices Some authorities, however, believe that the intake of water during meal time will dilute the digestive juices, therefore impairing the digestive processes The evidence in support of this belief is not convincing

ULTRASONIC RADIATION

To the Editor —*Can the operator of an ultrasound machine incur any ill-effects from giving these treatments over a long period?*

R S Lander, M D, Victoria, Texas

Answer —Consultation among four physicians, who have done much experimental work with ultrasonic therapy and who have used it extensively clinically, indicates that none of them has ever encountered any ill-effects, nor have they read of any ill-effects to an operator who administers ultrasonic therapy, even over prolonged periods Ultrasonic radiation can be transmitted through the soundhead to the patient only through a coupling medium, which is usually mineral oil or degassed water, and there is no transmission of the ultrasonic radiation to the operator, under these circumstances As far as can be determined, it may be said with fairly strong assurance that there is almost no likelihood of any ill-effects to the operator who uses such a machine

TIBIA VARA

To the Editor —*What are the signs of Blount's disease?* *Joseph H Grossman, M D, Shaker Heights, Ohio*

Answer —True tibia vara is manifested by bowing of one or both legs as a result of an acute angulation at the proximal tibial epiphysis It is not to be confused with other diseases which cause bowing in the shaft of the bone It must be differentiated clearly from a physiological deformity involving not only the proximal tibial but also the distal femoral and distal tibial epiphyses This physiological exaggeration of the normal will usually correct itself spontaneously The classification into infantile and adolescent forms refers only to the time of appearance

CONTACT LENSES

To the Editor —*Is there any evidence that contact lenses will alter the progress of myopia?*

William S Abbey, M D, Fort Collins, Colo

Answer —There is no reliable evidence that contact lenses will alter the progress of myopia

CEREBRAL PALSY

To the Editor —*Have any advances been made within the last few years in relation to the possible cure or arrest of cerebral palsy?*

Maurice M Hillman, M D, New Haven, Conn

Answer —Although extensive studies have been made in recent years of the various etiological factors of so-called cerebral palsy, there has been little advance in knowledge of any cure or arrest when a child is born with this disorder There have been advances in treatment with use of physical therapy, rehabilitation, orthopedic measures, and muscle relaxant drugs, but none of these can be interpreted as a cure With these advances in treatment, however, the outlook for a child with cerebral palsy is certainly much better than it was at one time

JEWISH CARE OF NEONATES

To the Editor —*Can you give me information concerning the ancient Jewish care of neonates? Does it differ from the modern Jewish custom? How long were swaddling clothes left on the baby?* *A Veitch, M D, Lisbon, N D*

Answer —I am unable to find data on the duration of swaddling among Jewish infants A fine discussion of Jewish attitudes toward the care of neonates is found in Preuss' "Biblisch-talmudische Medizin" (Berlin, S Karger AG, 1921, p 468) Benedict has some data on swaddling in her paper "Child Rearing in Certain European Countries" (*Am J Orthopsychiat* 19 342 [April] 1949)

DIABETES AND TRAUMA

To the Editor —*Would you please let me know if any cases have been reported in which trauma, especially to the lower thoracic segment of the spine, has resulted in precipitating diabetes mellitus?* *R S Lander, M D, Victoria, Texas*

Answer —Various authors have claimed that diabetes followed injuries, including those to the trunk, but, as far as this consultant is aware, there is no case on record in which trauma to the thoracic segment has been followed by diabetes

ABSTRACTS FROM THE LITERATURE

American Journal of Diseases of Children

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Cloud Baby '—In a detailed study of the mechanisms of spread of staphylococci in nurseries, the authors observed that the majority of newborn babies with nasal colonization had a low index of infectivity A minority, called cloud babies because of the clouds of bacteria surrounding them was an important factor in the causation of explosive outbreaks of staphylococcal infection and disease both in the nursery and within the family unit after discharge The cloud baby is clinically well and can be recognized at present only through the use of quantitative air sampling techniques Microbiologic investigations revealed that the factors responsible for cloudiness consisted of various common respiratory viruses occasionally encountered in hospitalized newborn babies These cloud factors operated independently of the staphylococci and had a distinct epidemiology of their own

Idiopathic Epilepsy in Early Infancy—A proportion of children with mental deficiency have also various types of epileptic attacks In such instances the most frequent denominator of these 2 disorders is cerebral damage, malformation, or metabolic disturbance However there seems to be a small group of infants in whom frequent, minor attacks occur as a manifestation of idiopathic epilepsy It appears that if the epileptic seizures of this type commence during initial months of life mental retardation may result as a consequence of frequent attacks Analysis of the history as well as clinical and laboratory findings in 6 such infants tends to corroborate this hypothesis Brief reference was made to the definition of idiopathic epilepsy and to the treatment of spasms with hypsarrhythmia by ACTH and cortisone

Survey of School Children for Cystic Fibrosis—A simple and rapid screening test for the detection of cystic fibrosis was made in 3 036 school children attending kindergarten and the first 4 lower grades of 8 schools in Worcester Mass This test is based on the presence of high salt concentration in the fingers and palms of patients with cystic fibrosis The plate test gave 2 8 per cent false positive readings in the initial mass screening test with less than 7 per cent false positives on a 2nd examination and no positive reactions on the 3rd and final reading All children with a positive test on 2 occasions were studied clinically and were subjected to more definitive tests to rule out cystic fibrosis Some of the factors which influence the test results have been reviewed Although no patients with cystic fibrosis were uncovered by this survey, its value for survey purposes is discussed We recommend, as a result of this experience, that initial positive reactors be retested at least twice prior to their selection for more definitive clinical and laboratory investigations

Primary Erythrocytosis of Childhood—A 6 year-old boy with a hemoglobulin level of 27 8 Gm per 100 cc, a red blood cell count of 9 25 million, and a hematocrit of 78% was studied for the cause of his erythrocytosis No evidence of hypoxia or a vascular shunt could be found, and normal white blood cell count and platelets eliminated the diagnosis of polycythemia vera Family studies suggested a mild form of the disease in the parents and 2 siblings Only minimal evidence could be found for increased red cell production, but red cell survival by the chromium ^{51} technique showed an increased half-life of 39 days The findings suggest that some property of the erythrocytes in this case alter the rate of elution of the chromium or, perhaps, that decreased destruction of the red cells may be responsible for the erythrocytosis

Pulmonary Function Studies in Children—Eleven hundred sixty-three apparently healthy school children, 624 boys and 539 girls were studied to provide standard values for the estimation of normal vital capacity, maximum expiratory flow rate, and timed vital capacity The ages ranged from 6 to 14 years Fifteen per cent of the population was in the adolescent period Prediction formulas were determined for vital capacity and maximum expiratory flow rate The formulas for vital capacity are as follows for male children, $VC = 86\ 64 \times$ age in years $+ 25\ 09 \times$ height in centimeters -2364, for female children, $VC = 84\ 22 \times$ age in years $+ 22\ 45 \times$ height in centimeters -2077 The formulas for maximum expiratory flow rate are as follows for male children, $MEFR = 8\ 366 \times$ age in years $+ 0\ 064 \times VC$ in milliliters $-50\ 646$, for female children, $MEFR = 8\ 77 \times$ age in years $+ 0\ 059 \times VC$ in milliliters $-49\ 38$ Nomograms were constructed for both the vital capacity and maximum expiratory flow rate values

Mental Retardation and Muscular Dystrophy—In our series of children with the primary diagnosis of pseudohypertrophic muscular dystrophy comprehensive psychological evaluations established that this group is functioning at intellectual levels significantly below those expected for normal children A review of the literature concerning the relationship of mental retardation to pseudohypertrophic muscular dystrophy reveals a wide variance in the findings of different investigators as to the presence or absence of mental retardation Our study of 30 patients revealed a mean I Q of 82 Fifteen of the patients had I Q s below 95 The mean for this group was 61 No relationship could be established between degree of mental retardation, degree of functional ability, or the age of onset of the clinical disease This study demonstrates that *significant mental retardation* may occur in individuals with muscular dystrophy to a greater extent than can be explained on the basis of emotional factors alone

Alcaligenes Faecalis Infection —Bacterium alcaligenes was isolated in 2 fatal cases of pneumonitis, 1, associated with meningitis in the newborn period, has been reported in the present paper The 1st infant weighed 2 kg (4 lbs , 3 oz) at birth, and at delivery had moderate cyanosis, marked hypotonia, and rapid, labored respiration At 1 week of age, lumbar puncture showed a polymorphonuclear pleocytosis but culture of spinal fluid was negative for bacteria Penicillin and streptomycin were given On the 11th day of life, the baby became cyanotic and lapsed into semi-coma In the next 48 hours the abdomen became distended, there was guaiac-positive vomitus Chest x-ray showed irregular densities bilaterally, consistent with *pneumonia* Digitalis, gamma globulin, cortisone, chloramphenicol, and erythromycin were given Electrolytes were administered intravenously to correct a metabolic acidosis Whole blood transfusion was given on the 14th day because of falling *hemoglobin* level, but the baby died next day Necropsy revealed resolving bronchopneumonia in all lobes, necrotizing esophagitis, and acute meningitis The 2nd patient weighed 1 25 kg (2 lbs , 12 oz) at birth, was cyanotic at delivery, and required resuscitation Respiration was irregular and labored, there was hepatomegaly X-ray of the lungs the next day was normal Penicillin and streptomycin were given parenterally At 60 hours, sclerema of lower extremities was noted, this progressed to involve the entire body Respiration became more rapid and labored, and ceased at 87 hours of life Necropsy showed hyaline membrane formation and confluent bronchopneumonia in all lobes Bacterium alcaligenes faecalis was isolated in pure culture from blood of both babies during life At postmortem, a similar organism was recovered in pure culture from heart's blood and cerebrospinal fluid in Case I, and from left and right lower lobes of lungs and spleen in Case II

Cat-Scratch Disease I Epidemic Occurrence —The epidemic of cat-scratch disease in the Minneapolis–St Paul area is the 3rd recognized epidemic of cat-scratch disease, the 2nd recognized in North America In the 1st year, 12 cases developed between October, 1955, and February, 1956, in the 2nd year, 6 cases occurred between September, 1956, and January, 1957 All cases of cat-scratch disease reported in North America were reviewed and a similar fall and winter preponderance noted About 90 per cent occurred during the months of September to February

Cat-Scratch Disease II Family Epidemics —Cat-scratch disease was observed in epidemics of 2 or 3 cases in 4 families, and in single cases in 4 other families Both groups were similar in that 3 of the 4 families had 1 or more additional family members with positive cat-scratch skin tests Among the 38 apparently well family members, 10 (26 4%) had positive cat-scratch skin tests indicating an asymptomatic infection Attack rate, clinical cases, and positive reactors, totalled 24 of a possible 52 (46 1%) All families had cats aged 3 to 7 months at the time of onset of the index case This observation is probably explained by the fact that young and playful kittens scratch frequently Cases occurred as late as 48 days after the last cat contact In the family epidemics, the interval between cases varied from 3 to 61 days

Cat Scratch Disease III Intradermal Skin Test —The specificity of the intradermal skin test with cat-scratch disease antigen was evaluated in 6 groups (1) Well members of families with 1 or more cases of cat-scratch disease had an incidence of 10 of a possible 38 (26 4%) (2) Well members of families of patients ill with a disease other than cat scratch disease had an incidence of 2 of a possible 37 (5 4%) (3) Hospitalized children without clinical cat scratch disease had an incidence of 6 of a possible 119 (5 1%) (4) Outpatient and hospitalized adults without evidence or history of cat-scratch disease had an incidence of 4 of a possible 50 (8%) Both group 5 (veterinarians) and group 6 (physicians) had an increased incidence of positive skin tests The general population, groups 2, 3, and 4, had 5 8 per cent positive reactors, therefore, a positive cat scratch skin test has a confidence level of about 95 per cent

Deafness in Children Due to Ossicular Defects —Hearing loss in some children is due to defects in the ossicular chain Defects may be congenital or due to myringotomies, infection, or mastoid surgery The eardrums may be normal These children hear better by air than by bone conduction By a *comparatively minor surgical procedure* the eardrum can be elevated and the continuity of the ossicular chain restored This may require mobilizing the stapes, gluing ossicles together, or replacing the stapes with an artificial *prosthesis* Hearing was restored in 3 children One had a congenitally fixed stapes, another, a defective incus, due to myringotomy, which was corrected by adhering the stapes to the incus with bone glue The 3rd had an absent incus due to mastoid surgery, and the stapes was glued to the eardrum

Gastric Acidity in the Prematurely Born Baby —The purpose of this study was to measure the gastric acidity of the prematurely born baby during the first 10 days of life The 6-hour fasting gastric juice of 58 babies with birth weights of 1,000 to 2,200 grams (2 to 4 5 lbs) was analyzed for free and total hydrochloric acid The result showed no significant difference in the average amount of acid secreted on the 1st and 10th days of life, however, the highest average was obtained on the 4th day On the 1st day 12 of 58 had more than 20 units free acid and 19 had none Three of the 19 secreted no acid on any of the 10 test days Neither birth weight, gestational age, nor sex affected the titratable acid of the 10-day acid curve except that boys on the average secreted more acid than did girls

Infants Fed Soybean and Evaporated Milk Formulae —*In an attempt to compare the nutritive value of soybean* (Mull Soy) milk and evaporated milk formulae in early *infancy*, several *moieties* of growth and various biochemical determinations were documented in comparative groups of normal-term infants fed either soybean or evaporated milk formulae from birth to 3 months of age Gains in weight and length, as well as the *patterns* of increase in weight and length, were similar in both study groups Hemoglobin and hematocrit values were comparable in both study groups, and in a 3rd group of control infants fed an ad libitum diet Plasma biochemical determinations (sodium, potassium, chloride, cholesterol, total protein, and protein fractions) were comparable at birth and at 3 months with 2 exceptions (1) a significant increase in the total plasma cholesterol at 3 months in infants fed evaporated milk and ad libitum diets, and (2) a marked fall in the level of gamma globulin in all patients at 3 months

Diastematomyelia—A case report is presented of an infant with a small myelomeningocele, who developed scoliosis because of vertebral anomalies and asymmetry of trunk musculature The cause of death was aspiration pneumonia after application of a cast Autopsy showed diplomyelia from the 1st thoracic to the 3rd lumbar vertebra A bony and cartilagenous spicule separated the 2 halves of the spinal cord at the 1st lumbar vertebra The cord showed duplication of the central canal at those levels where diplomyelia was evident The anterior and posterior horns were not duplicated The anomaly is discussed according to Bremer s explanation of persistence of the neurenteric canal The importance of the case lies in the pathology of an entity with varied clinical manifestations and anatomical expression There is a great scarcity of anatomical–clinical studies of such cases in the literature

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Graduate Surgical Education in Community Hospital—The general surgical residencies in the community and medical center hospitals are compared A group of community hospitals in the North Central area of the United States was analyzed It was emphasized that there is a need for the community hospital in the training of the general surgeon The excess of positions in the surgical residency program and the large percentage of graduates of foreign medical schools filling such positions was again pointed out The need for increasing interest in research, either basic or clinical for the development of a true educational program and for a sufficiency of cases for the ward service are facts which must be faced by the community hospital The various methods of attaining these may be 1 or more of the following a director of medical education, a direct affiliation with a medical school, or a more vigorous approach by the surgical staff

Edglugate-Mg as a Blood Preservative—Blood, taken up to 4 days prior to its use for extracorporeal perfusion, was preserved by using Edglugate-Mg Clinical experiences in 69 patients, using 637 units of blood are encouraging and warrant continued use of this anticoagulant-preservative When not used for perfusion blood preserved by this method can be given as routine transfusions to other patients The increase in plasma potassium with storage was 8 8 mEq/L (1 day), 11 7 mEq/L (2 days), 13 6 mEq/L (3 days), and 13 3 mEq/L (4 days) For perfusion of patients weighing less than 25 kg either freshly drawn blood or blood with serum potassium less than 10 mEq/L should be used Plasma hemoglobin levels were within tolerable limits in blood up to 4 days after being drawn

Ischemia, pH, and Renal Damage—In a search for better means of diagnosis, prognostication, and treatment evaluation in acute renal damage a series of experiments was carried out with isolated perfused dog kidneys subjected to varying periods of ischemia and varying pH of the blood perfusate The levels of cellular moieties in the perfusate and urine were used as indices of disrupted cell integrity By use of a 3-dimensional graph it was shown that the amount of cellular enzyme loss during 60 minutes perfusion was independent of the time of ischemia (between 20 and 120 minutes) and was minimal at pH values from 6 5 to 7 7 In the pH range of 7 7 to 7 8 large amounts of enzyme were lost It was concluded that urinary enzyme studies may not be of value where the predominant etiology is vasospasm reduced blood volume, or ischemia from other causes, but this approach may assist in delineating some of the so called toxic factors in renal damage, 1 of which appears to be alkalosis

Third Kidney Phenomenon of Gastrointestinal Tract—Under certain circumstances large-volume aspirate from the gastrointestinal tract has been demonstrated to reflect the volume of parenteral infusate This may well result in a leapfrogging phenomenon in which larger amounts of fluid are given to cover larger losses until huge exchanges have been achieved Whether or not obstruction existed was important In the absence of clinically significant obstruction the process was resolved simply by cutting down on the intravenous ration Large-volume exchanges attendant on organic obstruction usually require a secondary operation for correction Recognition and correction of serious metabolic deficits should be maximally achieved prior to secondary operation as the patient s condition is often critical

Hemodialysis in Surgical Patients—Hemodialysis was performed on surgical patients with renal failure both pre- and postoperatively A parallel flow MacNeill dialyzer and blood pump was utilized in an extracorporeal vein to vein circuit Three uremic patients with obstructive uropathy were rapidly prepared for surgery by a solitary dialysis 24 to 48 hours prior to their operative procedure Postoperative and post-trauma acute renal failure were managed by a rigid medical regime and the aid of 1 to 3 hemodialyses The primary indications for dialysis were hyperkalemia marked acidosis, and clinical deterioration as evidenced by persistent emesis, lethargy, and convulsions The survival rate was greatly influenced by coexisting surgical complications In a group of 12 patients with no major complications, 9 patients survived In contrast, 1 out of 9 renal failures associated with multiple injuries and sepsis survived

Cardiac Output in Response to Surgical Trauma —To obtain a greater understanding of the stress placed upon the circulation by trauma and its relation to the known alterations in endocrine and metabolic activity, observations were made on 45 patients who underwent major pulmonary, cardiac, or abdominal operations In the normal uncomplicated course a pattern of circulatory response emerged which is divided into a phase of cardiac depression during the anesthesia and operation and a postoperative phase of elevated cardiac output and reduced peripheral arterial resistance All of the patients showed a depression of cardiac output well below the preoperative basal value after induction of anesthesia which was accompanied by a rise of venous pressure and total peripheral resistance This was more pronounced during thoracotomy At the time of endotracheal extubation, a significant elevation of cardiac output occurred By contrast, all 6 of the patients who failed to exhibit this phenomenon died subsequently Postoperatively the patients who had laparotomies maintained cardiac outputs at or slightly below their mean preoperative cardiac index of 3 0 L/sq m/min, while those who underwent thoracotomy sustained an elevated mean cardiac index of 3 5 L/sq m/min for a week or more Although the trauma of major surgery does not place a great demand upon the circulation, inability to meet the basal demands of the tissues for perfusion results in progressive acidosis and death, as illustrated by the courses of 6 patients who died with low postoperative cardiac outputs

Spontaneous Regeneration of 7th Nerve —Spontaneous return of facial function has been noted in an occasional patient who has had the facial nerve resected at time of cancer surgery The question has been raised as to the mechanism of this reinnervation of the facial muscles of expression Ten puppies had their 7th nerve divided at the stylomastoid foramen along with a wide resection of the peripheral branches Those which recovered were subjected to a series of experiments with the following conclusions (1) Spontaneous return of facial function can occur after wide excision of the 7th nerve in dogs (2) Experiments failed to show that the reinnervation was due to take over by the contra-lateral 7th nerve or to anastomosis of the 7th and 5th nerve endings (3) It was the final conclusion that reinnervation in the dog was due to regrowth of the 7th nerve fibers

Neck Dissection for Cervical Lymph Node Metastases —For many years the treatment of cervical lymp node metastases from oral carcinoma has been the operation of radical neck dissection The so-called prophylactic neck dissection, formerly questioned, is now regaining popularity A study has been done on 68 patients who have had radical neck dissection during the period 1950 to 1956, inclusive, with a minimum follow-up period of 3 years The complications and mortalities were noted as were the number of pathological positive nodes that were found The presence or absence of local recurrence of the primary tumor in the mouth at the time of death was also studied From this study the authors conclude that a more vigorous and radical attack should be directed toward the primary intra oral tumor, particularly where there is no evidence of cervical lymph node metastases Only after the primary lesion is well controlled should the full neck dissection be carried out

First Branchial Cleft Sinus —A persistent draining sinus from the 1st branchial cleft is quite rare, a total of 13 cases has been reported Two patients with this defect were operated upon The 1st patient was a 36-year-old white female who had 3 previous unsuccessful operations for a draining sinus of the neck The 2nd patient was a 6-year old boy with a draining sinus anterior to the ear Both patients were cured by dissection of the sinus tract to its origin in the auditory canal Details of the operative technique are illustrated with the relation of the sinus tract to the facial nerve

Total Thyroidectomy for Thyroid Carcinoma —The occurrence of multicentric foci of carcinoma is the principal reason for performing total thyroidectomy for carcinoma of the thyroid In our experience the over-all frequency of multicentricity was found to be at least 13 per cent In a group of total or near total thyroidectomies, the figure was at least 23 per cent In approximately half of the patients with multicentric foci, both lobes of the thyroid were involved Multicentricity was especially a finding in a significant number of patients under the age of 20 This evidence appears to justify total or near total thyroidectomy for most patients undergoing surgery to cure thyroid carcinoma Preservation of parathyroid tissue is feasible for nearly all patients If parathyroid tissue is not identified and preserved, it is usually preferable to leave a remnant of thyroid tissue in the region of the normal location on the side of the neck opposite the primary or predominant lesion

Toxicity Studies of 5-Fluorouracil in Surgery —Clinical studies demonstrated increased toxicity when the usual anticancer course of 5-fluorouracil was given as an adjunct to surgery These patients tolerated two-fifths of the prescribed course Animal studies discounted the significance of (1) surgery per se, (2) anesthesia, or (3) shock in the etiology of toxicity However, marked leukopenia occurred in animals deficient in caloric, vitamin B_6, or protein intake Moreover, gastrectomized rats receiving 5-fluorouracil plus 5% dextrose in 0 45% isotonic sodium chloride solution postoperatively were compared with control animals with similar surgery but fed rat pellets Eight of the 9 animals on parenteral fluids died, while 12 of the 13 in the control group survived These studies emphasize the importance of the patient's nutritional state when anticancer therapy is administered Potentiation in toxicity occurs when surgery and chemotherapy are combined in the presence of cachexia or when parenteral fluids are required for several days

New Tracheostomy Tube for Bronchial Secretions —Experience with the use of tracheostomy in the therapy of lower respiratory obstruction due to retained bronchial secretions has revealed that the conventional tracheostomy tube is inadequate for the needs of these patients Clinical data and pathological studies support this concept A recently described plastic tracheostomy tube which allows the patient to cough effectively through a free tracheal lumen was used in 17 patients Thirteen of these patients underwent tracheostomy for lower respiratory obstruction They varied in age from 1 day to 80 years Clinical observation and pathological study revealed less destruction of the ciliary lining of the tracheobronchial tree and virtual absence of bronchial plugging by secretions with the new tube These findings contrasted strongly with previous experience when employing the conventional tube As an additional advantage the new tube allows normal speech

Forgotten Problem of Chronic Empyema —Chronic empyema has truly become a forgotten problem This has resulted from the perpetuation of pessimism regarding the adequacy and advisability of using the available operations for the management of chronic empyema and the consequent delay of the application of these corrective procedures In our review of 98 patients with chronic empyema, 53 could not be accepted for operation because of intercurrent pulmonary or cardiac insufficiency nutritional debility, or other complications which occurred during an unnecessary delay period prior to operation Twenty-three of the 53 patients considered inoperable already had insufficient or incomplete thoracoplasties when reviewed Forty-one of 45 patients with advanced chronic empyema operated on by 1 of 4 major surgical approaches are considered cured Practically all chronic empyemas can be cured if operations are performed early and completely obliterate the pleural space

Hypothermia During Cardiopulmonary Bypass —During 3½- to 4 hour perfusions, at rapidly reduced levels of hypothermia, the arteriovenous oxygen and carbon dioxide differences and the peripheral resistances within the animal were found At the temperature range of 18 to 26 C (64 4 to 78 8 F) a marked depression in oxygen uptake by the animal was observed This was of such a level that, at a flow of only 25 cc per kilogram per minute, the arteriovenous oxygen difference was equal to that obtained at flows of normal cardiac output during the control period At the level of 17 to 14 C (62 6 to 57 2 F) removal of oxygen was so much depressed that the normal range of arteriovenous difference was reached only at a perfusion rate of 10 cc per kilogram per minute while at the range of 10 to 11 C (50 to 51 8 F) the arteriovenous oxygen difference was approximately ⅓ that recorded during the preperfusion period and the perfusion could be stopped for periods up to 15 minutes without damage The peripheral resistance at these 3 levels was 11 700 11,990, and 8,000 dynes The addition of chlorpromazine to a perfusion in which the body cooling had reached the level of 9 to 7 5 C (48 2 to 45 5 F) did not affect the oxygen uptake depression which was similar to that seen in other experiments, but it reduced the maximum peripheral resistance to 3,475 dynes The rapid dilution of the perfusate by the introduction of cold Ringer s solution at the hypothermic state resulted in a sharp drop in the peripheral resistance as compared to that observed with perfusions at similar temperatures with whole blood Adequate oxygen uptake was demonstrated by calculating the arteriovenous difference per minute as well as by noting the restoration of the electroencephalographic tracing after rewarming and reconstitution of the concentration of the blood perfusate had been accomplished

Trilogy of Fallot —Of 370 patients having surgery for congenital heart disease, 22 had trilogy of Fallot Eleven had relief of their pulmonary stenosis only This was done as a closed procedure in 3 and under direct vision using hypothermia in the remainder There was 1 death in 13 operative procedures Postoperative catheterization data available show considerable improvement in cardiodynamics The remaining 11 patients had both the pulmonary stenosis and atrial septal defect closed at the same procedure under direct vision with hypothermia Three of these patients died Catheterization data available postoperatively reveal that the survivors were cured It is the opinion of the authors that the latter procedure is the one of choice

Arteriovenous Anastomoses and Varicose Veins —A search was made for connections between the arterial and venous systems of the leg in an unselected group of patients with varicose veins With the patient under anesthesia and in the Trendelenburg position, the lumenal aspect of the varices was exposed and inspected, using the operation microscope (Zeiss) One or more vessels consistent with arteriovenous anastomoses (AVA) were found in 13 of 14 patients These tiny, thick-walled tributaries appeared to convey highly oxygenated blood under greater than normal venous tension into the affected vein These observations support the idea that AVA are concerned in the development of varicose veins In addition these experiences suggest that the operation microscope may become an important adjunct to surgery of the future

Chymotrypsin Dissolution of Intra-arterial Thrombi —Distal thrombosis secondary to arterial obstruction, extending to small vessels is refractory to treatment This clinic has studied the proteolytic and fibrinolytic effects of chymotrypsin on intra-arterial thrombi In these experiments the isolated extremity was perfused with oxygenated blood containing a high concentration of chymotrypsin in an attempt to dissolve intra-arterial sodium morrhuate thrombi Thirty-two extremities were perfused, and partial to complete lysis was seen in 100 per cent of the 24- to 48-hour thrombi and 66 per cent of the 72-hour thrombi Clot lysis was demonstrated by arteriograms, gross inspection, and microscopic analysis Significant changes in the fibrinogen, factor V factor VII, and prothrombin content were confined to the isolated extremity

Hepatectomy and Hepatic Necrosis —This study was undertaken in an attempt to define by electrophoretic methods the nature of the responses of the plasma proteins following surgical removal or cellular dysfunction of the liver Paper electrophoresis was repeatedly performed on plasma and serum samples from 60 dogs studied in 4 experimental groups including total hepatectomy, partial hepatectomy carbon tetrachloride (CCl_4) hepatic necrosis, and sham hepatectomy controls Following total hepatectomy in glucose supported dogs, an early characteristic alteration or shift in the electrophoretic mobility of the serum alpha globulins occurred which was accompanied by the appearance of increasing levels of free plasma hemoglobin Further studies by a continuous flow electrophoresis technique revealed the presence of a hemoglobin-binding protein (haptoglobin) as the major component of normal alpha$_2$ globulin which exhibited diminished electrophoretic mobility in the presence of the increased levels of free hemoglobin following hepatectomy With chronic hepatic cellular necrosis produced by carbon tetrachloride, a diminution or complete disappearance of the alpha globulin band occurred, suggesting a primary lack of production of serum haptoglobin by the diseased liver No specific changes in electrophoretic mobilities were noted following either 70 per cent partial hepatectomy or control sham hepatectomy

Hypotension in Obstructive Jaundice —In 350 patients with surgical jaundice hypotension followed by uremia was the most common complication which led to death A systolic blood pressure below 90 mm Hg for 2 hours or longer usually caused a rise in the blood urea nitrogen Studies in dogs confirmed the clinical suspicion that the kidneys in the presence of obstructive jaundice are more sensitive to hypotension Furthermore, hypotension occurred with very small blood losses in jaundiced dogs These findings strongly emphasize the need for preoperative blood transfusions and careful replacement of surgical and postoperative blood losses in the jaundiced patient Through a program directed toward preventing hypotension, the surgical mortality in jaundiced patients has been decreased The association of hypotension with uremia may help to clarify former concepts of the causes of death in patients with surgical jaundice

American Journal of Ophthalmology, Chicago

49 881-1086 (May, part 1) 1960 Partial Index

Spontaneous Choroidal Detachment
C M J Velzeboer p 898
Steroid Treatment of Corneal Opacification
G A McCoy and I H Leopold p 906
Ocular Manifestations of Narcolepsy
W P Keef, R E Yoss and others p 953
Glaucoma and Myopia
G Lugossy p 981
Retinal Hemorrhages in the Newborn
C L Giles p 1005

Ocular Manifestations of Narcolepsy —The narcoleptic tetrad consists of (1) excessive sleepiness or narcolepsy, (2) attacks of muscular weakness (cataplexy), (3) sleep paralysis, and (4) hypnagogic hallucinations The authors report ophthalmologic studies on 25 patients with narcolepsy, who were examined by neurologists and were referred for ophthalmologic study irrespective of the presence or absence of visual complaints Ten of the 25 patients had complained of intermittent diplopia, 9 had noted only blurring of vision while reading Five patients had noted neither diplopia nor blurring One patient had noted diplopia only during attacks of cataplexy In general, diplopia on reading was related to marked exophoria, while blurring of vision was associated with only moderate exophoria Narcoleptic patients may present themselves to the ophthalmologist with vague ocular complaints such as eyestrain, weak eyes, difficulty in reading, or tiring of the eyes when watching motion pictures or television Recognition by the ophthalmologist of the basic disorder of excessive sleepiness is of great importance since effective analeptic drugs are available to treat narcolepsy Methylphenidate (Ritalin) administered in doses of 20 mg 3 or 4 times daily will control the excessive sleepiness of most patients When the patient is maintained in a state of normal alertness his visual difficulties disappear

Glaucoma and Myopia —On the basis of 4 case histories the author demonstrates that the recognition of glaucoma may be readily missed in myopic patients During refraction the examination of the fundus is frequently difficult because of a dim vision in the center of the crystalline lens When the causes of visual deterioration are sought glaucoma should be taken into consideration as well as myopia and cataract Special care is imperative in cases in which the vision cannot be fully corrected with lenses Not infrequently dimness of sight due to phacosclerosis gives rise to misinterpretation of the condition, and the real cause of poor vision, the glaucoma, remains undiscovered Thus, the possibility of glaucoma should always be considered in the presence of myopia When glaucoma is discovered too late, or not at all, removal of a cataract is of little or no use as far as improving sight is concerned If the glaucoma is discovered in time, the patient should be informed about the effect of pilocarpine, so that he will not neglect instillation

Retinal Hemorrhages in the Newborn —This report is concerned with 100 full-term newborn infants who were subjected to ophthalmoscopic examination within 1 hour after birth Infants in whom retinal hemorrhages were found were examined at 24-hour intervals until the disappearance of the retinal hemorrhages (or until the time of discharge) and those with negative findings were followed for 48 hours The parity of the mothers, premedications used, duration of labor, anesthetics employed, method of delivery, weight of infant, degree of cyanosis, and the findings of the ophthalmologic examination were recorded The over-all incidence of retinal hemorrhages was 40% The parity of the mother, weight of the infant, duration of labor, anesthetic agents employed, and degree of cyanosis at birth could not be implicated as major causes of retinal hemorrhages in the infants Rapid release of the increased intracranial venous pressure as a result of poor delivery of the head of the infant seems to play a significant part in determining the presence of retinal hemorrhages

Annals of Internal Medicine, Lancaster, Pa

52 949-1176 (May) 1960 Partial Index

Water Diuresis in Adrenal Cortical Insufficiency
A E Thomson, E G Brownell and G R Cumming p 949
Acute Renal Failure in Asiatic Cholera
C Benyajati and others p 960
Treatment of Toxic Nodular Goiter
M Eller and others p 976
Subacute Granulomatous Thyroiditis
F U Steinberg p 1014
Group A Streptococci in Acute Glomerulonephritis
S H Bernstein and M Stillerman p 1026
Mild Pulmonic Stenosis
S M Ayres and D S Lukas p 1076

Treatment of Toxic Nodular Goiter —Of 1,603 patients with hyperthyroidism who were treated with radioactive iodine (I^{131}) at the Mount Sinai Hospital, New York, between 1945 and 1954, 436 had toxic nodular goiter One hundred twenty-seven of the 436 patients had solitary nodules Seventy-eight patients (18%) were men and 358 (82%) were women Eighty-one patients (20%) were less than 40 years of age The patients with toxic nodular goiter were considerably older than those with toxic diffuse goiter Ninety-two per cent of the patients with toxic nodular goiter were cured with radioactive iodine, and 8% were made permanently myxedematous, the percentages were identical among the patients with toxic diffuse goiter Patients with toxic nodular goiter required an average total dose of 10 3 mc of I^{131} and an average of 2 2 treatments each, as compared with a total dose of 7 2 mc of I^{131} and an average of 1 9 treatments for toxic diffuse goiter This represents the differences in uptake and size of gland, rather than in radiosensitivity Eighteen per cent of the patients with toxic nodular goiter had some degree of exophthalmos as compared with 32% of those with toxic diffuse goiter Auricular fibrillation was observed in 25% of the patients with toxic nodular goiter and in 10% of those with toxic diffuse goiter Radioactive iodine is effective in the treatment of toxic nodular goiter

Subacute Granulomatous Thyroiditis.—The clinical picture of subacute granulomatous thyroiditis was 1st described by Quervain in 1904. The disease has shown a considerable rise in incidence, possibly because the correct diagnosis is made more frequently. The cause is not known. It may be caused by a virus infection, possibly by transmission from the upper respiratory tract. There is increasing evidence that subacute thyroiditis may be an auto immune disorder, characterized by sensitization of the patient against his own thyroid gland. Symptoms consist of fever, painful localized swelling of the thyroid gland, and signs of mild hyperthyroidism. The most outstanding laboratory finding is a reduced radioactive iodine uptake associated with a normal or an elevated protein-bound iodine concentration. In severe cases the protein bound iodine concentration may show a transient drop. This is associated with a stage of clinical hypothyroidism. Recovery is spontaneous. It can be accelerated in some patients by radiotherapy or administration of adrenocortical steroids.

Archivio italiano di urologia, Bologna

32:405-482 (April) 1960. Partial Index

Remission of Intractable Pain in Inoperable Carcinoma
R. Passera p. 453
Reticulosarcoma of Kidney
G. Di Muro p. 471

Remission of Intractable Pain in Inoperable Carcinoma.—A technique of transorbital leukotomy, developed by the Italian surgeon Fiamberti for relief of intractable pain in inoperable carcinoma of the bladder, is described. It consists in reaching the white substance of the prefrontal lobe through the thin orbital roof and cutting into the thalamofrontal fibers to the necessary length and depth. The standard procedure comprises 6 cuts for each hemisphere, it takes only a few minutes and may be carried out under either local or general anesthesia. This psychosurgical procedure interrupts the conduction, and the perception by the patient, of abnormal impulses from the subcortical zones. Three men with vesical neoplasia and a woman with vulvovaginal leukoplakia were subjected to this form of treatment. The 4 patients experienced remission of pain, without any alteration of their affective and mental power. Survival ranged from 3 months to 3 years, with the patients remaining relaxed and tranquil in the family environment. The relief from pain allowed the elimination or considerable reduction of analgesics, which contributed to the well being of the patients.

Beitrage zur klinischen Chirurgie, Munich

200:257-384 (no. 3) 1960. Partial Index

Changes of Vertebral Column in Neurofibromatosis
W. Schulte-Brinkman and H. Mallinckrodt p. 257
Symptomatology and Pathology of Mesenteric Sarcoma
H.-J. Thormer p. 301
Periureteritis Plastica
W. Brosig p. 313
Symptomatology and Therapy of Synovioma
H. Greissinger p. 326

Mesenteric Sarcoma.—The author reports on a 48-year-old man and on 2 women, aged 48 and 46 years, with sarcoma of the mesentery who were operated on at the surgical clinic of the University in Leipzig, Germany. A myxofibroliposarcoma, the size of a man's head and weighing 26½ lb. (12 kg.), which occupied the entire left abdominal cavity and extended below the descending section of the mesocolon, was removed from the man. The postoperative course was uneventful, and 5 years after the operation the patient was in good health and did not show any signs of recurrence or of metastasis. A myxofibroliposarcoma of 8½ lb. (4.4 kg.) was removed from the 48-year old woman, who also made a rapid and uneventful recovery and was free of recurrence and metastasis 3 years after the operation. A fibroliposarcoma of 17½ lb. (8 kg.) which compressed a loop of the jejunum was removed and the compressed intestinal loop was resected in the 3rd patient. Intestinal atony, bronchopneumonia, and cardiac failure caused the patient's death on the 5th postoperative day. Autopsy revealed metastases of the mesentery and of the retroperitoneal fatty connective tissue. Rapidly growing, oversized abdominal tumors may be due to sarcoma of the mesentery. Their correct diagnosis may be difficult since they may not be considered in the differential diagnosis because of the rarity of the condition. Symptomatology and possibilities of clinical and roentgenographic differentiation from other abdominal and retroperitoneal tumors have been discussed. Laparotomy should be performed even if inoperability may be suggested by the size of the tumor and the reduced general condition of the patient. Radical removal of the mesenteric sarcoma is frequently possible because of a tendency to a relatively late occurrence of metastases.

Periureteritis Plastica.—The author reports on 5 men and 2 women, 21 to 70 years of age, with periureteritis obliterans or plastica (ureteral compression from an extrinsic source). In some of these, who were operated on at the surgical clinic of the University in Frankfurt am Main, the cause of the disease could be recognized with great probability, in contrast to reports in the literature according to which the etiology is unknown. One of the patients had a history of pancreatitis which resulted in necrosis of adipose tissue in the retroperitoneal tissue, healing occurred with scar formation associated with impairment of the ureter and kidney. In a 2nd patient pancreatitis could also be assumed to be the cause of the periureteritis since the Staub-Traugott phenomenon was observed clinically and a chronically contracted gallbladder was found on surgical intervention. Hematogenous metastasization similar to that observed with perinephritic abscess was considered to be the cause of the periureteric scar formation in a 3rd patient. Still another patient had a history of tuberculous spondylitis resulting in a gravitation abscess. Hydronephrosis occurred because of compression of the ureters due to perispondylitic granulation tissue formation. Impairment of the ureters in the presence of an infiltrative process in the small pelvis occurred after diverticulitis in 1 patient. Still other disease processes, such as organized hematomas after kidney injuries, urine infiltration, tumor metastases and cicatricial changes after roentgen irradiation in women with gynecologic diseases and operations may produce similar disease aspects, periureteritis obliterans therefore should be considered rather as a symptom than as a disease proper.

Symptomatology and Therapy of Synovioma.—The author reports on a 51-year-old woman with a synovioma near the left ankle, of 4 years' duration. The tumor had increased slowly in size and had shown symptoms of chronic inflammation. It was found to be painful on pressure and the skin temperature over the tumor was increased. On standing, and when the ankle was put into motion, the patient complained of mild dragging pain Roentgenograms of the ankle showed relatively diffuse decalcification zones A tentative diagnosis of a specific tendon-sheath hygroma was made and the patient was operated on Microscopic examination of the operative specimen revealed a synovial sarcoma Amputation of the leg was refused by the patient A local recurrence of the tumor was observed 12 days after the operation and the patient complained of pain in the groin Roentgen irradiation of the ankle and the groin was employed with satisfactory response Shortly thereafter a new local recurrence with ulceration was observed, and chest roentgenograms revealed metastases in both lungs The patient's general condition deteriorated rapidly and she died 9 months after the surgical intervention Synoviomas are malignant tumors of mesenchymal origin Their areas of predilection are the joints of the lower and upper extremities Due to their slow growth and local inflammatory symptoms they may easily be confounded with unspecific or specific inflammations They have a tendency to cause early pulmonary metastases Early diagnosis and radical treatment are of utmost importance Diagnosis may usually be established only on histological findings Biopsy should be performed and a tourniquet applied to avoid dissemination Rapid histological examination is essential Positive findings require immediate amputation

Journal Bone & Joint Surgery, Boston

42A 375-564 (April) 1960 Partial Index

Reconstruction of Thumb After Traumatic Amputation
C E Nemethi p 375
Spondylosis of the Cervical Spine
P Teng p 392
Unrecognized Trauma in Infants and Children
D H Altman and R L Smith p 407
Pyogenic Osteomyelitis and Arthritis of the Spine
B A Waisbren p 414
Hematogenous Pyogenic Vertebral Osteomyelitis
A Garcia, Jr and S A Grantham p 429
A New Bone Affection Feathering
H M Frost p 447
Microchemical Study of the Developing Epiphyseal Plate
R E Kuhlman p 457
Flexor Pollicis Longus Muscle
U Mangini p 467

Unrecognized Trauma in Infants and Children—The authors report on 5 infants, 1 month to 18 months of age, who were admitted to the Variety Children's Hospital and the Jackson Memorial Hospital in Miami, Florida, with traumatically-induced bone lesions Although a history of trauma was unobtainable in some of these patients on admission, subsequent studies provided strong indirect evidence in each to indicate that trauma was actually the predisposing factor The roentgenographic evidence of trauma was very obvious in some of the patients, in whom a fracture in 1 or more long bones or flat bones could actually be demonstrated In others the subtle metaphysial fractures were not so obvious Although a shaking or twisting type of injury will produce metaphysial infractions, more severe aggression, such as striking or throwing a child, may well result in frank long or flat bone fractures The diagnosis of traumatic injury to young bones should be made with a relative degree of certainty on the initial roentgenographic examination and confirmed by survey films of the long bones The recognition of trauma induced by adults or older siblings will save considerable time and effort in an attempt to arrive at a diagnosis The early recognition of the condition may be lifesaving, since removal of the child, if at all possible, from the environment in which these injuries occur should result in complete cure Close co-operation with enlightened juvenile authorities can be invaluable

Pyogenic Osteomyelitis and Arthritis of Spine—The authors present a preliminary report on 4 men and 3 women, 33 to 71 years of age, and one 14-year-old boy with proved or presumptive diagnosis of non-tuberculous, pyogenic osteomyelitis and arthritis of the spine who were treated with a combination of antibiotics and human gamma globulin at the Milwaukee County General Hospital A satisfactory clinical response to this therapy was obtained It is suggested that certain patients with this disease who are not responding to conventional methods of therapy may benefit from the administration of combinations of antibiotics (such as penicillin, streptomycin, chloramphenicol, erythromycin, vancomycin) and gamma globulin and that prolonged maintenance therapy with antibiotics may be necessary to prevent recurrence

Hematogenous Pyogenic Vertebral Osteomyelitis—The authors report on 24 male and 16 female patients, 3½ to 78 years of age, with hematogenous vertebral osteomyelitis who were treated at the New York Orthopedic Hospital, Columbia-Presbyterian Medical Center, New York In each patient the presenting complaint was back pain, frequently with nerve-root pain The principal physical findings were painful muscle spasm and limited motion of the spine Occasionally an angular kyphos or signs of psoas irritation were detected Positive neurological findings were often borderline or absent The often subtle and subacute nature of the disease has been emphasized The laboratory findings in many patients showed a high erythrocyte sedimentation rate with a normal or slightly elevated leukocyte count Frequently the lesion was not demonstrable by roentgenogram early in the disease Eventual spontaneous interbody fusion was the rule Twenty-seven of the 40 patients were treated by absolute rest in bed, often with additional plaster or brace immobilization Eight patients underwent incision and drainage of abscesses Laminectomy was performed on 2 patients with an erroneous diagnosis of epidural abscess Fusion at the level of infection was performed on only 3 patients The beneficial results obtained by immobilization in comparison with those occurring after surgical intervention have been emphasized Optimum treatment should include accurate bacterial studies followed by therapy with the appropriate antibiotic, rest in bed and immobilization Despite the long morbidity there was minimum residual disability

Lancet, London

1 933-988 (April 30) 1960 Partial Index

Jejunal Biopsy in Adult Celiac Disease
D J Fone and others p 933
Thyroiditis and Cirrhosis of Liver
B McConkey and P Callaghan p 939
Familial Glomerulonephritis and Amino-aciduria
I R Wallace and J H Jones p 941
Paromomycin in Shigella and Salmonella Infections
H M T Coles and others p 944
Assessment of Urinary Phosphate Excretion
B E C Nordin and R Fraser p 947
Leucine and Pellagra
C Gopalan and S G Srikantia p 954

Jejunal Biopsy in Adult Celiac Disease—The authors performed jejunal biopsies on 58 patients with idiopathic steatorrhea, or "adult celiac disease," in the General Hos pital, Birmingham, England In 27 patients (group 1) the appearances were uniform, with absent villi, epithelial disorder, and mild to moderate cellular infiltration, mainly with plasma cells In 27 other patients (group 2) the villi were present but abnormal in shape, the epithelial disturbance was less severe and the cellular infiltration was usually heavier In the remaining 4 patients (group 3) the villi were normal Clinical features and laboratory findings indicate that the cases of the patients in group 1, with absent villi, are etiologically distinct from the rest It is suggested that the condition in this group be called celiac disease or adult celiac disease, and that these terms be confined to patients with this lesion The histological appearances in the patients of group 2 may represent more than 1 etiological disorder For this group there is at present no satisfactory name

Familial Glomerulonephritis and Amino aciduria —The authors report on a family consisting of parents and 6 children, with occurrence of glomerulonephritis in 3 of the children who died as a result of the disease A 4th child died in infancy of an unknown cause The 2 surviving children and the parents in this family all had abnormal aminoaciduria which may have been due to inherited or acquired abnormalities of the renal tubules It is suggested that in this family an inherited defect responsible for amino aciduria also predisposes to glomerulonephritis It is important that families with a tendency to renal disease should be recognized and investigations of apparently unaffected members undertaken to exclude any renal defect

Paromomycin in Shigella and Salmonella Infections —The authors gave paromomycin, a new antibiotic derived from a strain of streptomyces, a therapeutic trial in 37 children admitted to Queen Mary s Hospital for Children in Carshalton, England Of these 9 had dysentery due to Shigella sonnei, 18 had symptomless infection caused by Sh sonnei 8 were in the convalescent stages of infection caused by Salmonella paratyphi B and 2 had symptomless infection caused by Sal typhimurium Paromomycin was given orally in a daily dosage of 40 mg per lb (80 mg per kg) of body weight In 8 of the 9 children with Sh sonnei dysentery and in 17 of the 18 carriers of Sh sonnei, stools were bacteriologically negative after short courses of paromomycin Five of the 10 excretors of Salmonella, similarly treated had negative stools No serious toxic reactions or superinfections developed Two reisolated strains of Sal paratyphi B showed partial drug resistance

Nederlands tijdschrift v geneeskunde, Amsterdam

104 709 756 (April 9) 1960 Partial Index

Chronic Cough and Eosinophilic Bronchitis in Lung Cancer
P J E Rouing and N G M Orie p 709
Conservative Treatment of Humerus Fractures in Patients Over 40
F Vaas p 713
Staphylococcic Diarrhea in a Surgical Ward
P A Ykelenstam p 720

Cough and Eosinophilic Bronchitis in Lung Cancer —The history of patients with lung cancer often reveals that cough existed long before it could have been caused by the tumor The authors review data on 100 patients with lung cancer (89 men and 11 women) whom they observed at a hospital in Groningen from 1953 to 1955 A group of 100 surgical patients most of whom were treated for trauma served as controls These 2 groups were compared as regards the incidence of chronic cough, single or repeated attacks of pneumonia, recurrent bronchitis, smoking habits, and the familial occurrence of asthma or chronic cough Chronic cough was 3 times as frequent in patients with pulmonary carcinoma than in the control group According to literature reports, chronic cough is caused by chronic eosinophilic bronchitis with or without infection An investigation carried out among the chronic cough cases in the lung cancer and control groups revealed the presence of eosinophilic bronchitis in 85% of the former group Among the carcinoma patients, twice as many persons smoked 10 or more cigarettes a day as in the control group In a study of the relationship between smoking and bronchial carcinoma, attention should be paid to chronic eosinophilic bronchitis If this exists, the etiological, preventive, and therapeutic consequences should be considered

New England Journal of Medicine, Boston

262 1099-1148 (June 2) 1960 Partial Index

Soybean Goiter Report of 3 Cases
T H Shepard and others p 1099
Apnea After Administration of Succinylcholine
H M Rubinstein and others p 1107
Middle Lobe Atelectasis Due to Sarcoidosis
G J Goldenberg and R H Greenspan p 1112
Myoglobinuria After Acute Arterial Occlusion
H I Horowitz J Javid and S H Zuber p 1116

Soybean Goiter —The authors report on 3 baby girls in whom goiters occurred when they were placed on soybean formulas In the 1st patient the goiter was detected by the mother after 1 month, in the 2nd patient the physician noted the goiter after 3 months, and in the 3rd patient the thyroid enlargement was not noted until after 39 months The 3 patients were euthyroid as judged by physical findings and normal growth Values for serum protein-bound iodine concentration were slightly low The radioactive iodine (I^{131}) uptakes were high, and became normal when soybean milk feeding was discontinued The goiters became much smaller or disappeared in 2 patients when soybean milk feeding was discontinued and in the 3rd when iodine was added to the diet Concerning the pathogenesis of soybean goiter the major amount of evidence seems to support an iodide-deficiency type of goiter The commercial product of soybean milk given to the 3 patients did not contain any added iodide Thyroid avidity for I^{131} was observed in 2 patients The microscopic appearance of the thyroid gland in the 1st patient showed increased cellularity, absence of colloid, and a few small follicles, i e, a picture similar to that reported in newborn infants in iodine deficient areas

New Zealand Medical Journal, Wellington

59 177-225 (April) 1960 Partial Index

Sequelae of Caesarean Section
H P Dunn p 180
Repeat Operations for Mitral Stenosis
D Robb p 183
Medico Legal Aspects of Epilepsy
G Glasgow p 187
Hematemesis and Melena Due to Peptic Ulcer
P B Herdson p 193

Repeat Operations for Mitral Stenosis —Of 203 patients who underwent valvotomy for mitral stenosis at the Green Lane Hospital in Auckland New Zealand, up to December 1959

6 male and 15 female patients had repeat operations and 1 of them had 2 repeat operations Two more patients have been recommended for repeat operations, making the total for repeats 24, or 11 8% The first operation had resulted in an inadequate opening of the valve In 19 patients the difficulty lay in the valve itself which was tough, fibrous, and unyielding to the finger or to cutting instruments, or was so distorted by calcific deposits as to remain too rigid to work well, even if the commissures were separated well or fully In 3 patients the difficulty lay in the approach access to the left atrium Of the 22 repeat operations, the valve was fully restored in 5, it was adequately opened in 13, and it was inadequately opened in 4 The clinical results obtained by the patients from the 22 repeat operations were excellent in 1, satisfactory in 17, and 4 patients died Recurrent mitral stenosis remains a difficult situation, but good results may be expected from valvotomy performed with the aid of the more recent technical maneuvers, such as the use of transventricular dilator Morbidity and mortality are not prohibitive Repeat operations, however, should become steadily rarer as the higher standards aimed at and the improved methods available result in better valve function after the 1st operation The present series represents the partial or complete failures of earlier efforts

Plastic and Reconstructive Surgery, Baltimore

25 455-546 (May) 1960 Partial Index

Cleft-Palate Patients and Their Speech
A R Vim Coff p 496
Homografting Between Identical Twins
J B Patterson p 510

Homografting Between Identical Twins—The author reports on a 5-year-old girl whose gown caught fire while she was standing by a butane cooking stove and who sustained a 68% full thickness burn for which she was hospitalized She is alive today by virtue of the fact that she had an identical-twin sister The patient was resurfaced with a total of 660 square inches of skin Of this total, 570 square inches were homografts taken from the twin who was used as a skin graft donor, and 90 square inches were autografts Coverage was started 22 days after the patient was burned and completed 17 days later Her period of hospitalization from time of injury to complete coverage and ambulation was 52 days

Revista médica de Chile, Santiago

88 157-246 (March) 1960 Partial Index

Acute Renal Insufficiency in Septic Abortion
C Villavicencio and others p 177
Recurrent Acute Pericarditis
J Ahumada L Niedmann, and A Illanes p 190

Acute Renal Insufficiency in Septic Abortion—Twenty-seven patients (their ages ranging from 17 to 32 years) were treated for acute renal insufficiency developed in the course of a septic abortion In 19 patients the toxemia was caused by Clostridium perfringens, and in 8 it was secondary to septic abortion of a different etiology There was hemolytic complication in 18 patients, 9 of them were treated with exsanguination transfusion, 2 with hemodialysis by artificial kidney, and 4 with the usual treatment for renal insufficiency Ten of these patients recovered, 3 died before they could receive any treatment, and 5 died in spite of extra-renal hemodialysis Of the 8 patients without hemolytic complication, 7 were treated by the usual method, and 1 with combined transfusion-artificial kidney treatment Only the latter patient died, not of renal insufficiency but of colon pyemia Anemia and cardiovascular collapse were considered the main factors in renal insufficiency associated with septic abortion Hemolytic complications play an important role in the course and prognosis of the condition Treatment of the hemolytic forms should consist of massive exsanguination transfusion and control of the electrolyte imbalance Only when these measures fail should the procedures of extra-renal hemodialysis be applied Use of the artificial kidney is then the treatment of choice

Semaine des hôpitaux de Paris, Paris

36 865-924 (March 24) Partial Index

Congenital Tuberculosis Due to Tuberculous Endometritis
M Kaplan and others p 865
Antipoliomyelitis Vaccination of the Infant
R Grumbach and others p 889

Congenital Tuberculosis Due to Tuberculous Endometritis—The authors report on a premature female infant in whom congenital tuberculosis was detected 1 month after birth The purely pulmonary localization of tuberculous lesions suggested infection by inhalation The endometrial biopsy specimen obtained from the mother revealed latent tuberculous endometritis which was primary and which was the only tuberculous lesion Microbacterium tuberculosis was found in the infant and in the uterus of the mother Clinically the infant's condition at first seemed to be favorably influenced by intensive antibiotic treatment, but she died at the age of 4 months and 25 days from respiratory and cardiac insufficiency Chest roentgenograms visualized complete destruction of the right lung Autopsy showed that destruction of the parenchyma was actually bilateral and was, therefore, incompatible with survival There were numerous abnormal spaces in the lungs, some representing emphysematous sacs, and the others cavities without caseation The lungs also exhibited granulomatous metaplasia and hypertrophic or atrophic reticular pneumonia There was, however, complete bacteriological sterilization of the lungs at the time of the infant's death

Semana médica, Buenos Aires

48 355-386 (March 31) 1960 Partial Index

Spinal Lesions in Children s Tetanus
E Sujoy p 355
New Antiparkinsonian Preparation
R Castelluccio p 372

New Antiparkinsonian Preparation—Experimental treatment with a glutaric acid derivative (Aturban) was given to 15 patients, 12 of whom had paralysis agitans (Parkinson's syndrome), 2 had congenital tremor, and 1 had choreo athetosis Each patient received a 5-mg tablet 3 times a day during 3 months The therapy was effective, especially in relieving rigidity, tremor, and walking difficulties, with less marked effect on speech and ocular disorders The improvement of the patients' morale was evident in 66% of this series Tolerance to the drug was excellent The maximal daily dosage for this group of outpatients was established at 20 mg, but under hospitalization higher dosage might be tolerated Symptoms reappeared on interruption of the treatment, in some patients more markedly than before The drug (3-phenyl-3[β-diethylaminoethyl]glutarimide hydrochloride) is considered superior to others in its effect on tremor

WASHINGTON NEWS

Committee Approves Voluntary Health Bill
Senate Debate
Red Tape Nightmare Seen
Eisenhower Views

FINANCE COMMITTEE APPROVES VOLUNTARY HEALTH PLAN

A voluntary, federal-state plan for helping the needy aged meet their health care costs cleared a third major hurdle in Congress, the Senate Finance Committee, and headed for a crucial vote by the full Senate

Six Democrats joined all six Committee Republicans in approving the House-passed health plan with some major modifications The same line-up soundly defeated three attempts by five committee Democrats to put over Social Security health schemes

The margin of victory for the voluntary, federal-state public assistance approach in the influential Finance Committee strengthened the cause of the medical and allied professions as well as the administration for the showdown voting in the full Senate However, the outcome was by no means a foregone conclusion

Democratic presidential candidate Sen John F Kennedy declared the Committee measure 'must be rewritten on the floor of the Senate before the Senate goes home This Congress should not adjourn before it enacts a comprehensive, adequate plan to meet medical needs' He called for a medical aid plan for the aged lacking what he termed a 'destructive, degrading means test" Sen Kennedy's running mate, Senate majority leader Lyndon B Johnson (Tex) also said the committee bill was inadequate

In addition to the House health plan, the Senate Finance Committee added a new provision authorized by Sen Robert Kerr (D , Okla) This would establish federal grants to help the states provide an extra $12 a month, strictly for medical care, for 2 4 million persons now receiving old age assistance The money would go into a special fund for this purpose, and the federal share would range from 50 to 80 per cent depending on the per capita income level of the state The states would have sole power to decide who would be eligible

The committee approved with slight changes the House health plan—a voluntary, federal-state cost sharing program to cover an estimated 500,000 to 1 000,000 persons not receiving old age public assistance but with inadequate finances to cover the cost of catastrophic illnesses or injuries

Total first year cost for the Finance Committee bill was put at $190 million

Finance Committee Chairman, Sen Harry F Byrd (D , Va), and ranking committee Republican Sen John J Williams of Delaware, predicted they would be able to guide the committee measure through the Senate intact

Although the committee bill differed in many respects from the plan advanced by the Administration, it avoided the social security route and was expected to receive support from most GOP members of the Senate

Voting for the bill in Committee were Democratic Senators Byrd, Kerr, J Allen Frear (Del), Russell B Long (La), George A Smathers (Fla), and Herman E Talmadge (Ga) The Republican members of the committee, all of whom approved the bill, were Senators Williams, Frank Carlson (Kan), Wallace F Bennett (Utah), John Marshall Butler (Md), Carl T Curtis (Neb), and Thruston B Morton (Ky)

Democrats pushing for a Social Security plan were Senators Clinton P Anderson (N M), Paul H Douglas (Ill), Albert Gore (Tenn), Vance Hartke (Ind), and Eugene J McCarthy (Minn)

Other changes made by the Finance Committee in the bill as cleared by the House included

Junking a provision that would have brought self-employed physicians and medical and dental interns under the Social Security program for the first time

Providing that Social Security recipients could earn $1,800 in outside income, compared with $1,200 at present

Allowing men to retire at age 62 and start drawing Social Security retirement, but at lower levels than with retirement at age 65 Women now have this option

Upping the maximum federal contribution under the federal-state medical aid plan for needy aged to 80 per cent, compared with the 65 per cent maximum in the House bill

SENATE OPENS DEBATE ON HEALTH CARE ISSUE

The controversy over various plans for health care of the aged spilled onto the Senate floor as the lawmakers opened full-scale debate on the important, election-year issue

Defending the voluntary plan approved by the Senate Finance Committee, Sen Robert Kerr (D , Okla) told the Senate that the plan could go into effect by October 1 in a large number of states I believe it can and will be accepted by the President,' he said In that event, we would have a great program for the aged needy of our country, and have it this year'

Sen Herman Talmadge (D , Ga) noted that under the social security health schemes Congress would compel every self-employed individual in America and every worker who is on social security to take out compulsory insurance Should Congress, the Senator asked, 'compel the people of the nation to go into the insurance business with the government?"

Disputing charges that the aged would have to undergo paupers oath" requirements under the Committee bill, Sen Russell B Long (D , La) said beneficiaries could "go to the hospital or go to the doctor and get whatever medical treatment they need

"After they had been in the hospital, whether it be a day or thirty days or a hundred days or a year, they would then simply sign a statement that in their opinion they were eligible to have their hospital bills paid under this program"

This is the way the medical care program already works in Louisiana, he said, noting that the individual states would be free to operate the program in any manner they see fit

Sen Long asked why the elderly should have their health care financed "by the most regressive type of taxation, taxation which hits most at the poor man and least at the rich," as would be the case under Social Security

Sen Long also said that under the measure "when the state puts up some of the money, that makes for a certain amount of responsibility on the part of someone who concerns himself with keeping down the amount of the bill, he tries very hard to avoid spending any more than necessary in the individual cases"

Urging adoption of a Social Security plan, perhaps even in addition to the entire Committee bill, were Senators Clinton P Anderson (D, N M), Hubert Humphrey (D, Minn), and Jennings Randolph (D, W Va) Sen Anderson said he thought the committee bill "does not go nearly far enough'

ASKEY WARNS OF RED TAPE NIGHTMARE

Dr E Vincent Askey, President of the American Medical Association, said any effort to finance the health care of the aged through compulsory federal insurance would "produce a red tape nightmare" He urged passage of the House-passed health care bill and rejection of a compulsory approach in any form

Speaking before the annual meeting of the American Pharmaceutical Association in Washington, D C, Dr Askey said, "under compulsory proposals, hospitalization, nursing home care, and surgical services would be authorized to all Social Security beneficiaries

"The people who would provide these services would be required to enter into agreements with the Secretary of Health, Education, and Welfare

"This would mean that the secretary would have to enter into agreements with some 7,000 hospitals, 12,000 nursing homes, and many thousands of physicians who could, if they liked, participate in the program It is possible that not all of these providers of services would sign-up—for no other reason than because of the time-consuming paper work which invariably attends such programs

"The problem becomes even more complex if bills of this kind include other benefits Depending upon the services authorized, HEW could also find itself in the position of negotiating agreements with 70,000 private nurses, 54,000 retail druggists, or 700 different visiting nurses associations

"Add to this the fact that the federal government would be required to control disbursement of funds, to decide the benefits to be provided, to set rates of compensation for hospitals, nursing homes, dentists, and physicians, to audit and control government expenditures to hospitals, nursing homes, and patients, and to establish and enforce standards of hospital and medical care

"In the process, can you imagine the forms to be filled out, the applications to be processed, the individual cases to be reviewed, the drug prices to be checked, the interminable correspondence going back and forth, the mountains of memoranda to be written, the jungle of red tape to be hacked through, the proliferation of bureaucrats to be expected?

"But there is another administrative structure in being which is readily available to do the job and capable of doing it well If a federal-state program were adopted, all that would be required would be a change in definitions to implement the provisions of the Mills House Bill

"If this measure became law, the negotiations required of the Secretary of HEW would be confined to each of the 50 states, all of which have well-established, functioning machinery to take over the responsibility of helping those of the aged who need help"

Dr Askey continued

"The American Medical Association has been trying its hardest to point out to Congress and the people of this country the fatal flaws in legislation of the Forand type At the same time, our association has sought to muster support for an effective, workable, measure to help those of the aged who need help in the financing of their medical care

"The Mills Bill, as passed by the House of Representatives and amended by the Senate Finance Committee, will help those who really need help And it allows those who *don't* need help to maintain their independence Furthermore, by calling for local administration, this program allows experts on the spot to tailor government help to individual need This is important because medical care is a personal thing, it cannot be mass produced, or administered at long range"

EISENHOWER RESTATES OPPOSITION TO COMPULSORY HEALTH PLAN

President Eisenhower again declared he is opposed to compulsory medical aid He told his weekly news conference he does not care if his plan to give help to the aged costs the treasury more than the compulsory Social Security program endorsed by the Democratic platform

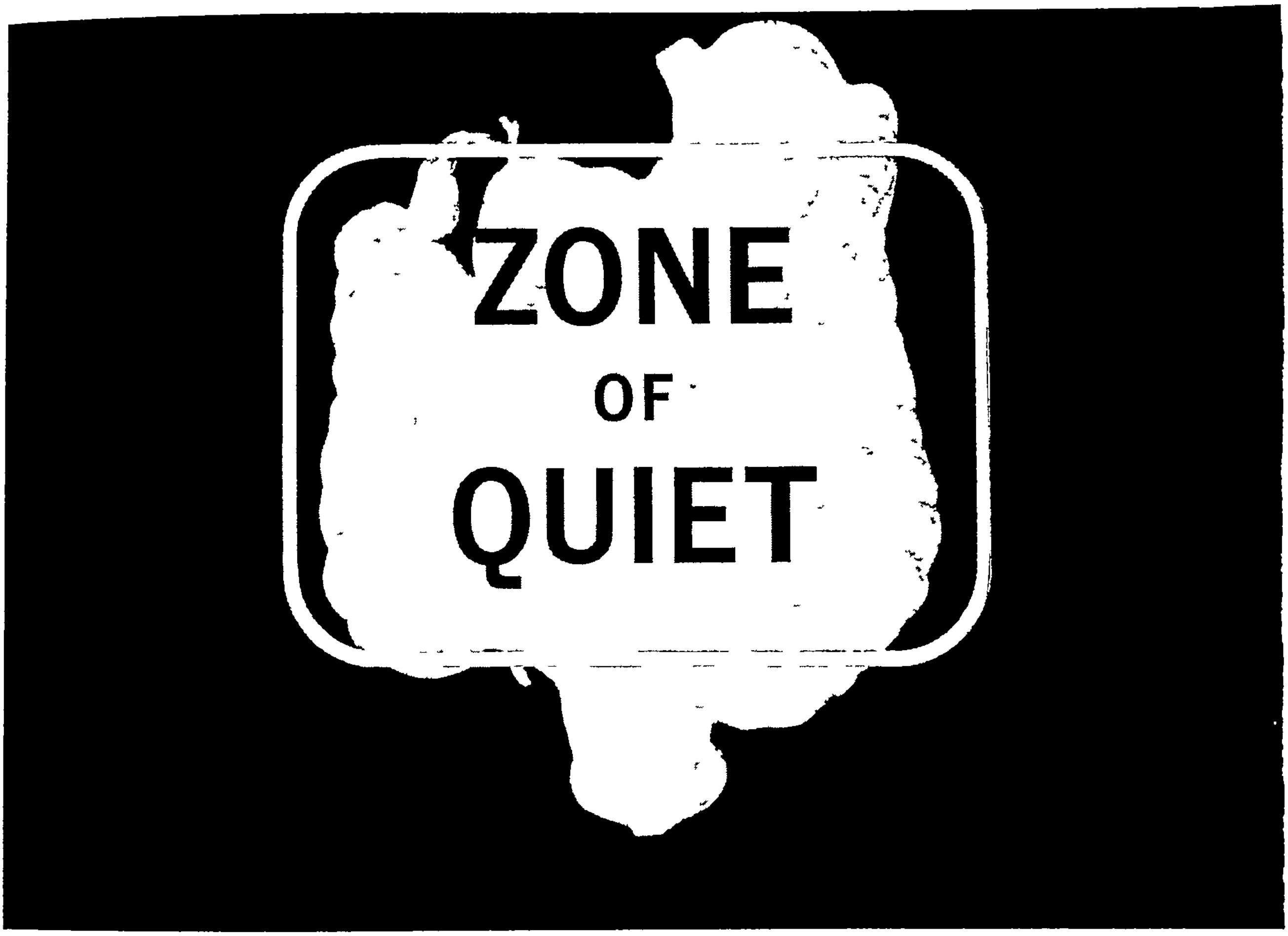
He gave this answer when asked why the Administration supports a medical care plan to be paid for out of general revenue instead of the Democratic plan that would be financed by a social security payroll tax

Mr Eisenhower said he favored a plan that would help the aged and still preserve freedom He said he was against what he termed compulsory medicine and did not care if his plan cost the government a little money Freedom sometimes costs money, he said

The Administration has recommended a system of Federal grants to the states out of general treasury funds to help pay for medical care of needy elderly persons

The President was asked his opinion of a proposal by former Welfare Secretary Marion Folsom to subject the medical care issue to further study and postpone action until next year

The President replied that he was a great admirer of Folsom, but believed that the issue already had been studied a great deal He said he was not against further study, but believed that action is needed now to help older persons pay medical expenses



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1 Henrickson W E : The Generalist Looks at Constipation GP *18* 128 (Oct) 1958

2 Bercovitz Z T : Medical Forum: Should Colectomy and Permanent Ileostomy Be Considered for Children with Ulcerative Colitis *Mod Med* 25 18 (July 1) 1957

3 Lumsden K and Truelove S C Intravenous Pro Banthine in Diagnostic Radiology of the Gastrointestinal Tract with Special Reference to Colonic Disease Brit J Radiol 32 517 (Aug) 1959

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1 Boger W P Strickland C S and Gylfe J M *Antibiotic* *Clin Ther* 3 378 (Nov) 1956 2 Boger W P In *Antibiotics* 1958-1959, New York, Medical Encyclopedia Inc 1959 p 4 U K Kulkarni B S, and Kamath P G *Antibiotic Med & Cl* 5 604 (Oct.) 1958 4 Anderson P C and Wissinger H A *U S* *Forces M J* 10 1051 (Sept) 1959

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Routine Immunization with Orally Administered Attenuated Poliovirus

A Study of 850 Children in an American City

Joseph S Pagano, M D, Stanley A Plotkin, M D, Carl C Janowsky, M D, Suzanne M Richardson, R N and Hilary Koprowski, M D, Philadelphia

In the United States, studies with living poliovirus vaccines have been conducted within institutions and families under ideal conditions The present study explored the feasibility of early immunization of normal children living in a low income area of an American city Most of the 850 children 1½ months to 6 years old entering the study were susceptible to poliomyelitis One, two, or three types of vaccine given orally at monthly intervals yielded significant antibody responses in 93 to 100% of children who had not yet lost maternal antibodies, and in 84 to 100% of children without antibodies Although this was not an evaluation of vaccine safety, community surveillance was maintained no case of poliomyelitis in Philadelphia occurred in a person vaccinated by this method or in his household The vaccines were efficacious, according to serologic evidence, in conferring immunity to poliomyelitis

RECENT epidemics of poliomyelitis in the United States have centered in the poorer sections of cities, the disease has principally affected children less than 5 years old[1] An increase in the incidence of poliomyelitis in Philadelphia, in 1958, when one-half the cases occurred in young children in the densely populated heart of the city, prompted the Department of Public Health to explore a new method of immunization A practical test of several strains of orally given poliovirus vaccine among children in an open community was designed as an important addition to the investigations of the action, effectiveness and safety of living attenuated poliovirus vaccines that have been conducted in the United States and abroad since 1949[2]

The need for immunization against poliomyelitis before 6 months of age and the difficulty of achieving it with Salk vaccine have been noted in both the United States and England[3] The efficacy of living attenuated poliovirus vaccines in conferring immunity against poliomyelitis in infancy, even in the presence of maternal antibodies,[4] suggested the choice of these orally administered vaccines

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From the Wistar Institute (Drs Pagano Plotkin and Koprowski and Mi Richardson) and the Philadelphia Department of Public Health (Dr Janowsky) Drs Pagano and Plotkin were associated with the Communicable Disease Center U S Public Health Service Atlanta

Methods and Materials

Design of Study.—The study was conducted from January to July, 1959, in 2 of the 10 health districts of Philadelphia, which were selected because 37 of the 77 cases of poliomyelitis (59 paralytic) in the city, in 1958, had occurred in them. The attack rate among the 50,000 children under 5 years of age in these districts had been approximately 62 per 100,000 as against the incidence of 28 per 100,000 among the 188,000 children under 5 in the city as a whole.

In the health centers where children were brought for free routine immunization, each child between 6 weeks and 6 years of age who had not received Salk vaccine was seen by a physician, who obtained consent from the mother for administration of the orally given vaccine. No other selection was made and over 95% of those eligible were entered in the study. A city health worker then interviewed the parent and recorded the age and address of the infant; during the study a record was also kept of blood specimens taken, vaccination dates, and illnesses.

Administration of Vaccine.—A health center nurse administered the vaccine. The strain of virus (see below), suspended in 1 cc. of phosphate-buffered saline solution (pH 7.0), was squirted into 1 oz. of milk in the infant's own bottle. Type 1 virus was given first, followed on two subsequent visits by type 3 and then type 2 virus respectively. Older children were given the vaccine in a cup of chocolate milk. During the day the virus suspensions ready for use were kept in ice water, and at night they were stored in the freezer compartment of a refrigerator not longer than four days.

Serologic Sampling.—The pediatric clinics held 13 meetings per week, 6 of which were selected at random as bleeding sessions; during these, the collections of data and vaccination were checked by us, and blood specimens were obtained by heel puncture from all the children to be vaccinated. These children were bled again on the final visit, approximately four weeks after administration of the last dose of vaccine.

Observations After Vaccination.—Return visits were scheduled at 4-week intervals over a 12-week period to coincide with diphtheria, pertussis, tetanus, and smallpox immunization, often performed on the same day the poliovirus vaccine was given. On each return visit inquiry was made about the health of the child, in particular whether there had been fever, diarrhea, headache, or vomiting; all illnesses, with dates of onset, were recorded. Recent hospitalizations of household members were noted.

Children who did not return as scheduled were visited within seven days by a public health nurse, the mothers were urged to return, and an assessment of the state of the child's health was made. If this procedure failed, the child was assigned for follow-up by a city health worker.

Surveillance of Poliomyelitis in the City.—Community surveillance was maintained through the City Department of Epidemiology, the State Virus Diagnostic Laboratory at the Children's Hospital of Philadelphia, and the health centers; each case of neuroparalytic disease or aseptic meningitis of possible viral etiology that was detected in Philadelphia was screened, and the possible cases of poliomyelitis were investigated by contacting the patient's physician.

Viruses Used for Immunization, Neutralization Tests.—The origin and characteristics of the strains of attenuated poliovirus used, CHAT (type 1), W-Fox (type 3), and P-712 (type 2), are fully described elsewhere.[5] They were prepared by the Wistar Institute—the P-712 from a virus seed lot provided by A. B. Sabin. The vaccine concentrations were 5.7 log tissue culture–infective doses$_{50}$ (TCID$_{50}$) CHAT, 5.7 log TCID$_{50}$ W-Fox, and 5.2 log TCID$_{50}$ P-712.

Neutralizing antibody titers were determined in paired pre- and post-vaccination serums from the same child (hereafter referred to as paired serums) by the metabolic inhibition test.[6] Random titrations revealed that all three vaccines declined in concentration by 1 to 2 log TCID$_{50}$ after they had been in use at the health centers for two or three days and had been thawed and refrozen several times.

Results

Description of Population.—Eight hundred and fifty type 1 vaccinations, 805 type 3, and 335 type 2 vaccinations were given. The series comprised 433 boys and 417 girls; over 90% of the children were Negroes. All three types of vaccine were given to 335 children, types 1 and 3 only to 470, and type 1 only to 45 children.

The age distribution, the cumulative percentages of vaccinated children at each age, and the distribution of bleedings is shown in table 1. Most of the children were less than 2 years old (79%), and over one-half (52%) were between 1½ and 6 months of age. Twenty-eight per cent were bled before vaccination so that a significant sample (about 20%) of paired serums would be obtained.

Vaccination extended over a 25-week period, beginning with CHAT type 1 on Jan. 13, which was given until the end of the 16th week (May 1), after which no new children were entered in the study. Type 3 vaccine was given until the 25th week (July 1). Administration of type 2 vaccination was discontinued in the 18th week because of a shortage of supply.

Health Inquiries.—A summary of the return visits and of the distribution of illnesses by weekly intervals after vaccination is shown in table 2. After receiving type 1 vaccine, 547 children remained well, and 16 could not be traced or were dropped because Salk vaccine had been given by mistake The balance of the 850 children had various illnesses, mostly simple colds without fever Gastrointestinal illnesses and fever unaccompanied by other symptoms were infrequently reported Exanthemas included chickenpox, measles, and rashes Miscellaneous illnesses were earaches (8), mumps (4), insomnia (2), wheezing (1), teething (1), pharyngitis (1), fretfulness (1), thrush (1), and not identifiable (1) Seven children were hospitalized, namely, four for pneumonitis, two for bacterial meningitis (pneumococcic and influenzal) proved by culture, and one for herniorrhaphy There was one death a 3 month old boy was found dead in his crib on April 10, 1959, five weeks after receiving type 1 and 10 days after type 3 vaccine, during which time the child had seemed perfectly well Post-mortem examination disclosed no gross abnormality Frozen specimens of the brain, medulla, and spinal cord yielded no virus in tissue culture, chick embryos, and mice Special histological stains failed to reveal lesions of the brain and cord The disposition of the coroner and of the consulting pathologist was sudden death of infancy of unexplained cause

TABLE 1 —*Age Distribution of Children Given Attenuated Live Poliovirus Vaccine*

Age	Vaccinees No	Vaccinees Cumulative %	Vaccinees % Bled Before Vaccination
1½ <2 mo	34	4	47
2 <3 mo	152	22	31
3 <4 mo	109	35	28
4 <5 mo	78	44	33
5 <6 mo	72	52	31
6 <12 mo	157	71	20
1 <2 yr	71	79	31
2 <3 yr	56	86	30
3 <4 yr	53	92	21
4 5 yr +	62	99	21
Unknown	6	100	33
All ages	850	100	28

TABLE 2 —*Condition of Children After Vaccination and Distribution of Illnesses by Intervals After Vaccination*

Vaccine Type	Interval After Vaccination Days	Post vaccination Record of Children: Kind and No of Illnesses											
		Cold	Cold and Fever	Exanthema	Fever	Cough	Gastro intestinal	Miscellaneous	Total	Well No	Delinquent No	Not Vaccinated No	Total
1	1 7	21	6	6	8	4	5	2	52	547	16		850
	8-14	24	6	5		3	4	4	46				
	15 21	40	2	2	1	1	3	4	53				
	22 28	39	16†	11‡	4	1	2	6	79				
	Other*	25	10	7	3	6	3	3	57				
3	1 7	16	3	4	8		6		37	550	39	45	850
	8 14	18	8	3			4	1	34				
	15 21	24	10	2	1		4	3	44				
	22 28	27	8	5	2	4	7	2	55				
	Other*	25	9	6	1	1	2	2	46				
2	1 7	1	3	1	2		2		9	251	16	515	850
	8 14	8	3	1	1			1	14				
	15 21	8	4	3		1			16				
	22 28	8	3		1	1	1		14				
	Other*	4	2	6		1	2		15				

* Includes illnesses occurring after 28 days and after an unknown interval
† Two from one district 14 from the other
‡ Three from one district 8 from the other

The incidence of illnesses was roughly similar during each of the four intervals after the administration of 1, type 3, and type 2 vaccine, except for a slight predominance during the 22- to 28-day interval, possibly because the mothers tended to recall the illnesses that had occurred during the period just before the clinic visit

TABLE 3 —*Distribution of Poliomyelitis Antibodies by Age of Children*

Age	Serum Titrations No	Negative Antibody Status Before Vaccination %: Triple	Type 1	Type 2	Type 3
1½ 3 mo	52	17	27	54	54
4 5 mo	20	60	75	85	80
½ <1 yr	17	82	88	94	100
1 <2 yr	16	62	81	100	81
2 <3 yr	11	55	91	82	73
3 <5 yr	10	40	60	80	80
All ages	126	44	58	70	67

Serologic Results

Before Vaccination —In analyzing the serologic response to vaccination, one must take into account the young age of the population (median, 6 months) with its expected high incidence of transplacentally acquired poliomyelitis antibodies[4] In the group 1½ to 3 months old, only 17% of the titrated serums were without any detectable antibodies (titer less than 1 8), and in only 27% were there no type 1 antibodies before vaccination (table 3) However, by the age of 4 to 5 months, the percentage of serums without antibodies had risen to 60%, a reflection of the rapid loss of transplacentally acquired antibodies Antibodies had dropped to non-detectable levels in virtually all children between ½ and 1 year old As shown in table 3, 82% of the serums lacked all three types of antibodies, 88% had no type 1 antibodies, 94% no type 2, and 100% no type 3 antibodies in this group Thereafter, the percentage of serums without any antibodies steadily declined until it was 40% in the 3-to-5 year group The percentages of serums lacking antibodies to all three types or to any one type of virus did not vary appreciably during the course of the study.

After Vaccination.—Vaccinations were judged successful if paired serums showed either a fourfold rise in titer or a change in titer from less than 1:8 to 1:8 (the latter applying to 11 serums). In addition, vaccination was considered successful in children less than 6 months old who had congenitally acquired antibodies if the observed titer after vaccination was at least four times greater than the expected titer at the end of three months. The predicted decline of maternal antibodies in three months was taken to be approximately 4 half-lives.[4]

TABLE 4.—*Summary of Success of Vaccination and Median Antibody Titers by Age and Susceptibility*

Vaccine Type	Age Group and Prevaccination Antibodies	Paired Serums, No.	Median Titers* Before Vaccination	Median Titers* After Vaccination	Outcome of Vaccination, % Successful (Fourfold Rise)†	Outcome of Vaccination, % Unsuccessful (Less Than Fourfold Rise)
1	1½ to 6 mo					
	Present‡	79	8	64	97	3
	Absent	22	<8	128	91	9
	(Total)	(101)	(8)	(64)	(96)	(4)
	6 mo to 6 yr					
	Present§	34	16	64	65	36
	Absent	32	<8	64	97‖	3
	(Total)	(66)	(8)	(64)	(77)	(23)
2	1½ to 6 mo					
	Present‡	30	16	64	93	7
	Absent	19	<8	64	100	
	(Total)	(49)	(8)	(64)	(96)	(4)
	6 mo to 6 yr					
	Present§	7	16	128	29	71
	Absent	25	<8	32	84‖	16
	(Total)	(32)	(8)	(32)	(66)	(32)
3	1½ to 6 mo					
	Present‡	63	8	64	100	
	Absent	31	<8	32	94‖	6
	(Total)	(94)	(8)	(64)	(95)	(5)
	6 mo to 6 yr					
	Present§	32	16	128	69	31
	Absent	32	<8	32	100‖	
	(Total)	(64)	(<8)	(64)	(78)	(22)

* If median titer occurred between two dilutions, lower dilution was taken as median. Titers expressed as reciprocals of serum dilutions.

† In some infants <6 mo. old with prevaccination antibodies, 4-fold rises were calculated by comparison with expected titer based on predicted decline of maternal antibodies (see text).

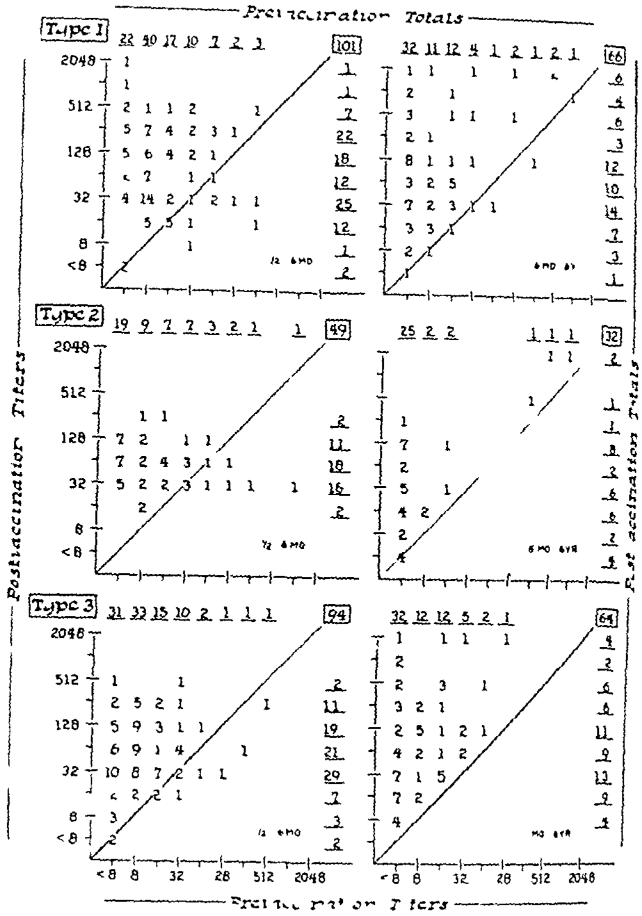
‡ Presumed to be of maternal origin.

§ Presumed acquired by natural infection.

‖ Includes 2, 2, 3, and 4 serums, respectively, with postvaccination titer of 1:8.

The patterns of antibody rises after vaccination are analyzed in table 4 and in the figure. Type 1 antibodies appeared in 91% of the children less than 6 months old who had lacked them. Significant levels of antibodies were also found after vaccination with type 1 in 97% of infants less than 6 months old that had had antibodies, thought to be of maternal origin, at the time of vaccination. A rise in type 1 antibody titer was observed in 65% of children more than 6 months old who had had antibodies, thought to be the result of natural infection, before vaccination. In contrast, as shown in table 4, 97% of children in the same age group without antibodies before vaccination had evidence of immunity after vaccination. The type 2 and the type 3 results in general showed similar rises, except that, in the 6-month- to 6-year-old group, fourfold rises in type 2 antibody titer were observed somewhat less frequently both in those without and those with antibodies before vaccination (rises of 84 and 29%, respectively).

The median titers for the 3 types, less than 1:8 to 1:16 before vaccination, rose to 1:32 to 1:128 after vaccination. There was at least a fourfold response in every group. In contrast, the median titer of 25 corresponding paired serums collected from children who did not receive type 2 vaccine remained less than 1:8 after vaccination.



Distribution of poliomyelitis antibody titers in children before and after vaccination by age group. Distribution of pre-vaccination antibody titers is given by pre-vaccination totals for each titer along tops of 6 boxes; post-vaccination totals are given for each titer along right sides of boxes. Above each pre-vaccination titer is vertical column of figures that indicates distribution of post-vaccination titers. Numbers above diagonal lines represent instances of increase in titer after vaccination, those on diagonal lines had same titer before and after, and numbers below diagonal lines represent instances of fall in titer after vaccination (e. g., box at upper left: there were 22 serums [top] with pre-vaccination titer of less than 1:8 [bottom, same column]). After vaccination, titers had risen (same column), so that there were four serums with titer of 1:32, two serums with titer of 1:64, and one serum at 1:2,048. Two serums remained at less than 1:8. In 1½- to 6-month age group pre-vaccination antibodies were assumed to be maternal in origin; in instances in which vaccination was unsuccessful, these antibodies would be expected to show decline in titer of more than 2 dilutions (see text).

Table 5 shows the distribution of the three types of antibodies in the same children before and after vaccination Before vaccination, serums from 33 children were without antibodies, after vaccination, 26 of these children had all three types of antibodies, and 7 had two types Of 14 children that had had antibodies of one type only, and of 3 that had had antibodies of two types, all except 2 children acquired the three types after vaccination Finally, none of those 12 children with the three types of pre-vaccination antibodies, which were in many instances maternal in origin, lost them afterward

Community Surveillance

Approximately 3,800 persons in 830 households—1,977 adults, 1,820 children less than 18 years old, and 991 children 5 years old or younger—were known to be in intimate contact with the vaccinated children

Table 5 —*Response to Vaccination of Children with Various Patterns of Susceptibility*

Antibodies Present Before Vaccination Types	Paired Serums* No		Antibodies Present After Vaccination Serums with 3 Types No	Serums with 2 Types No
0 0 0	33	→	26	7†
1 0 0	6	→	4	2‡
0 2 0	3	→	3	
0 0 3	5	→	5	
1 2 0	2	→	2	
1 0 3	1	→	1	
0 2 3	0			
1 2 3	12	→	12	
Entire group	62		53	9

* The completely titrated serums obtained from the 335 children given all 3 types of vaccine

† Two serums without type 1 antibodies 4 without type 2 and 1 without type 3

‡ Two serums without type 1

Between the end of January and the end of July, 1959, 97 cases of aseptic meningitis, encephalitis, and paralytic disease in Philadelphia were screened in the laboratory as possible cases of poliomyelitis On investigation, none of the 97 cases resembled poliomyelitis clinically and had laboratory evidence of poliomyelitis infection, none of these cases was considered to be poliomyelitis by the Department of Public Health The first isolations of poliomyelitis virus (type 3) were made in July, 1959, from the stools of two children in whom the onset of paralytic disease was, respectively, June 11 and June 19 A third case occurred on July 19 The three children, who were the only persons known to have contacted poliomyelitis during the study, lived in the study districts but were unvaccinated and did not live in households of vaccinated children Thereafter, 19 more cases of clinically verified poliomyelitis (16 paralytic) occurred during the remainder of 1959 in Philadelphia, 8 of them in the study districts, but none of them in vaccinated children or in their households Among these cases laboratory evidence of five type 3 infections and of four type 1 infections was obtained

Comment

This is the first study in the United States of the use of living attenuated poliovirus vaccine in a substantial number of susceptible children living normally within a large city Other investigations have been conducted in housing projects[7] and as household studies[8] This study, which made use of existing city public health facilities to incorporate oral poliovirus administration into the routine immunizations of infancy, was conducted in crowded areas of the city where most of the cases of poliomyelitis had occurred the previous year

Susceptibility of Population—Serologic analysis before vaccination indicated that there was a period of about 3 years—from approximately 4 months to 3 years of age—during which the children in this population were highly susceptible to poliomyelitis Sixty-six per cent of the serums obtained from children in this age group were without antibodies of any type We estimated (from the data in table 3) that of the 850 children, 493 (58%) did not have type 1 antibodies, 595 (70%) did not have type 2, and 569 (67%) did not have type 3 before vaccination, among these were 374 (44%) children without any poliomyelitis antibodies In addition, most of the children less than 4 months old that had maternal poliovirus antibodies before vaccination could be expected to become fully susceptible within two months, owing to the evanescence of transplacentally acquired antibodies, as indicated by the sharp increase in children without antibodies in the 4-to-5-month age group (table 3) The percentage of susceptible children tended to drop again at about 3 to 5 years of age, a reflection of the time at which natural immunity was probably acquired in this population (table 3)

Safety of Vaccine—The safety of the vaccine, both for the vaccinated children and for their contacts, was continuously scrutinized No case of poliomyelitis, paralytic or non-paralytic, occurred in a vaccinated child Beyond that, analysis of the minor illnesses occurring in vaccinated children indicated a random distribution We did not prove the safety of the vaccines, to accomplish this, appropriately controlled large-scale trials with larger numbers of susceptible children are required Several such trials are being conducted[9]

It seemed clear that illnesses in the vaccinated children could not be attributed to the vaccines or to a hypothetical contaminating agent, for had one of the vaccines been the cause of minor illness, a regular interval between administration of that type and the onset of a specific illness would have been observed in vaccinated children in both districts The type of illnesses reported—mostly common colds—did not seem attributable to vaccination Most of the children received what might be considered a provocative inoculation (diphtheria-pertussis-tetanus)[10] at the same time that they were given the orally administered poliovirus vaccine, without, however, any untoward effect

Was the vaccine safe for the community? The children came from about 830 households scattered through the heart of the city No case of poliomyelitis occurred in these households, although they included 991 children in a highly susceptible age group In addition, the study districts contained approximately 50,000 children less than 5 years old Although the children in this study may not be a completely representative sample of the children in the study districts, it can be estimated from the figures in table 3 that approximately 25,000 children in the districts were probably susceptible to poliomyelitis The three cases of poliomyelitis that occurred in Philadelphia during the study were consistent with the pattern of the disease, which has been seen early in previous poliomyelitis seasons, both in Philadelphia and in neighboring New Jersey Moreover, one of the three patients, while in New Jersey, had been in contact with children from whom type 3 poliovirus was isolated

Response to Vaccination—Vaccination effected a substantial rise in antibody titer against all three types of poliomyelitis virus in every age group, regardless of the previous state of immunity Occasionally, antibodies that were detected before vaccination may have originated by transmission from already vaccinated children, and some of the titers detected after vaccination may have been the result also of spread or of natural infection However, we surmised that these factors were probably not of great significance, because the susceptibility of children entering the study did not vary greatly, and because 92% of the children who did not receive type 2 vaccine did not have a rise in type 2 antibodies Children with transplacentally acquired antibodies responded to vaccination as well as did children without antibodies before vaccination

In children less than 6 months old, both with and without pre-vaccination antibodies, between 91 and 100% had a significant response to type 1, 2, and 3 vaccine Serologic evidence of immunity among susceptible children older than 6 months was observed after vaccination in 97% of cases for type 1, in 100% for type 3, and in 84% for type 2 In addition, children presumed to have naturally acquired permanent immunity frequently had an increase in antibody titer

The response of children given all three vaccine strains is of especial interest because it shows the likelihood of the formation of the three types of poliomyelitis antibodies in a child after vaccination (table 5) Eighty-five per cent (53 of 62) of these children had all three types of antibodies after vaccination compared with 19% (12 of 62) before vaccination In other words, few children were rendered immune to one type of poliovirus at the expense of remaining susceptible to another type When a course of Salk vaccine is given to children without antibodies, the results may not be as good[11]

Conclusions

The population recently shown by several urban epidemics to be most in need of immunization and least likely to get it are children less than 5 years old in the lower income groups[1] The crucial period of susceptibility occurs after most children are out of reach of agencies that provide the immunizations of infancy, but before the children enter school It is most desirable to immunize children against poliomyelitis before they are 6 months old However, with inactivated virus vaccine this is usually not done, because primary immunization is followed by third and then fourth inoculations after an interval of six months Furthermore, the presence of the higher titers of maternal poliomyelitis antibodies in infants tends to interfere with a good response to Salk vaccination, making it advisable to commence immunization at the age of 6 months[1] This and previous studies have shown that such difficulties can be circumvented, and that durable immunity against the three types of poliomyelitis virus can be achieved[12] with the orally administered poliovirus vaccines These living attenuated poliovirus vaccines appeared to be practical immunizing agents of high efficacy in conferring serologic immunity

Summary

Immunization with living attenuated polioviruses of infants and children living normally in a large city was essayed as a practical public health measure CHAT, type 1, vaccine was given to 850 children between 1½ months and 6 years old, 805 of these were also given W-Fox, type 3, and 335 were given P-712, type 2 vaccine, in sequence Serologic sampling disclosed that 44% of the children were without any poliomyelitis antibodies before vaccination, 66% of those 4 months to 3 years old lacked antibodies of all three types before vaccination The illnesses uncovered during the study appeared unrelated to vaccination None of the 22 cases of poliomyelitis in Philadelphia, in 1959, occurred in vaccinated children or in their households Of children less than 6 months old, 91 to 100% had a significant antibody response to the type 1, type 2, or type 3 vaccine Children more than 6 months old who had no antibodies before vaccination responded with a fourfold rise in titer in 84 to 100% of instances The proportion of children with antibodies to all three types of virus was increased from 15 to 85% after vaccination

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Dr John J Hanlon, Director of the Department of Public Health, City of Philadelphia, fostered this study Many persons in the department participated Sylvan Fish, M D, Rotan Lee, M D, the late Angelo Perri, M D, Lois Ham mond, M D, Lewis Polk, M D, Mark Whitman, M D Cornelius Stephany, M D, Katherine Levine, M D, Ralph Zaroff, D O, Robert Frazier, D O, Stanley Orons, D O, Esther Brown R N Margaret Cooney, R N, Patricia Di Muzi, R N, Evelyn Eby, R N, Ethel Taylor, R N, William Powe, Cogley Jones, and Martin Stamm Elmer Hall Statistics Section, Communicable Disease Center, assisted in the statistical analysis, Nancy Schnerr, Ph D, Mary Sanford, and William Fairbairn, Computing Center University of Pennsylvania, helped in the tabulation of the data Klaus Hummeler, M D, Children s Hospital of Philadelphia, conducted the laboratory aspects of the community surveillance Laura Randall helped in the preparation of the manuscript We acknowledge with pleasure their invaluable contributions

The views expressed in this study are those of the authors and are not endorsed by the U S Public Health Service

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GOITER-PRODUCING FOODSTUFFS —The evidence for the existence of naturally occurring goitrogens is firm thiocyanates and thiouracil-like substances occur in plants eaten by domestic animals and, to a much lesser extent, in foods eaten by man It seems that a thiocyanate could be responsible for a significant amount of goitre in lambs when the ewes are fed certain plants Experiments so far conducted have excluded the possibility that a thyroid-blocking substance may also be responsible It is highly unlikely that plant foods rich in thiocyanates are eaten in sufficient quantities to produce goitre in man At least one thyroid-blocking agent occurs in foods eaten by man, but since these are eaten cooked, and cooking prevents the formation of the active form, it is highly unlikely that this substance, obtained directly from the plants is a factor The possibility that goitrogens might be acquired from milk has been explored The evidence is inconclusive and still of an indirect nature One possible goitrogen γ-methylsulphonyl propylisothiocyanate, has been isolated from a cruciferous weed which is known to be eaten by cows in a district where there is a high incidence of goitre in human beings A goitrogenic substance has not yet been isolated from the milk, although the investigations are proceeding Epidemiological studies of children in goitrous regions, some of whom have been given prophylactic iodine for a number of years, strongly suggest that a goitrogen probably present in the milk is responsible for much of the thyroid enlargement especially for the seasonal epidemics of goitre —F W Clements M D Naturally Occurring Goitrogens *British Medical Bulletin*, May, 1960

Soft Tissue Roentgenography

Its Use in Diagnosis of Thyroid Carcinoma

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Among six patients who were proved at operation to have carcinoma of the thyroid three were found in whom the preoperative roentgenographic findings would have sufficed to give the diagnosis In each of these three cases psammoma bodies were found in sections of the carcinoma One out of four patients with local recurrences of thyroid carcinoma also showed characteristic malignant calcifications In a total of 45 patients studied by soft-tissue radiography there were no false-positive diagnoses In the differential diagnosis by roentgenography it is borne in mind that malignant calcifications are not dense but are poorly marginated, approximately uniform in size, grouped in streaks or in nebular formation, and without a calcific rim

A prolonged and, at times, even violent disagreement has arisen over the management of thyroid nodules In the treatment of nodular goiter, it is now generally agreed that the emphasis should be on the diagnosis of the thyroid nodule and that operation should be performed early if the possibility of cancer is high and conservative treatment administered otherwise Any technique that will, without risk, aid in the detection of carcinoma in patients with a nodular goiter will be a welcome addition to the present diagnostic armamentarium

In cystic tumors of the ovary, flat plate roentgenograms of the abdomen may reveal soft tissue calcifications which are due to psammoma bodies and are indicative either of cystadenoma or cystadenocarcinoma [1] Some carcinomas of the stomach and kidney present the characteristic soft tissue calcifications on roentgenographic examination,[2] as do some meningiomas [3]

In 1958, Holtz and Powers[4] published a retrospective study on calcifications in 53 patients with papillary carcinoma of the thyroid Twenty-eight patients had routine roentgenograms, which included those of the neck, available for review, three of these had calcifications in the thyroid gland thought to be typical of carcinoma In one, the diagnosis of papillary carcinoma was made preoperatively on the basis of roentgenographic findings The authors clearly delineated the differentiation between benign and malignant calcifications in the thyroid gland (see criteria below) We had been using soft tissue radiography as a preoperative diagnostic aid for lesions of the breast[5] Because of our favorable experience in this area, we decided, in November, 1958, to apply this method to lesions of the thyroid gland There were, at that time, no published criteria for the diagnosis of early carcinoma of the thyroid gland It was our hope that we would be able to differentiate preoperatively between benign and malignant tumors of the thyroid The criteria we derived independently agree with those of Holtz and Powers

Technique for Soft Tissue Roentgenography of Thyroid

Eight-by-ten cassettes with par speed screens and extension cones are used throughout All exposure factors are given for a neck measuring 10 cm in the lateral diameter For each additional centimeter of neck measurement an additional 2 kv is used Three views are taken, and an extension cone is used

For the lateral view, the cassette is placed so that its bottom edge is located 1 in below the sternoclavicular joint The patient is placed in an upright position The mass or nodule is centered horizontally on the cassette, a right lateral view is used if the mass is located on the right and a left lateral view if the mass is on the left The patient is placed 6 ft away There is an exposure of 54 kv for 40 ma -sec non-Bucky

For the tangential view the patient is placed upright in an oblique position so that the mass is in relief and at the midpoint of the film The neck must not be twisted, the chin remains aligned with

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From the departments of medicine, radiology, and surgery and the Andre Meyer Department of Physics, of Mount Sinai Hospital the sternum The right posterior oblique view is used if the mass is located on the right side and left posterior oblique view if it is on the left side The tube is tilted 10 degrees cephalad, so that the principal ray enters the center of the mass or nodule at an angle of 10 degrees This throws into relief portions of the isthmus which may be hidden by the shoulders There is an exposure of 54 kv for 50 ma-sec The patient is placed 40 in away, and Bucky is used

The anterior posterior view is least important and is taken to show tracheal deviation or infiltration The patient is positioned for a routine anteroposterior view of the neck The principal ray is centered to the midlength There is an exposure of 55 kv for 50 ma-sec The patient is placed 40 in away, and Bucky is used

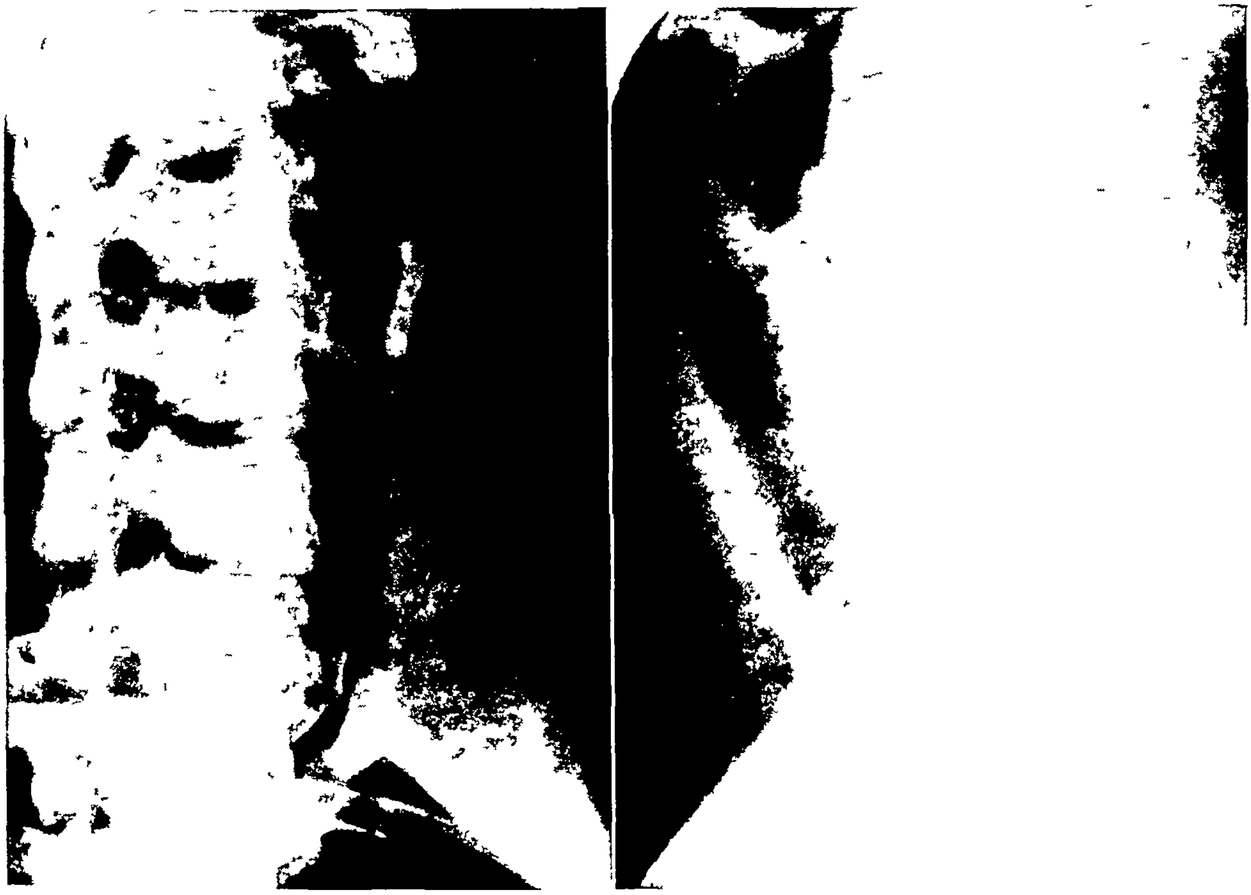

Fig 1 —*Left,* roentgenogram showing poorly marginated densities which are hazy, especially in large area subtended, and calcifications which are similar in size and density Diagnosis was malignancy (case 1) *Right,* in thyroid area are streaky, poorly marginated, similar sized calcifications of poor density, circumscribed in area, with no surrounding calcific rim Diagnosis was carcinoma (case 2)

Case Material—Originally, all patients scheduled for thyroid surgery from the private practices of the authors were examined prior to operation according to the roentgenographic technique described These patients had been selected for operation on the basis of history and physical examinations In almost all instances, radioactive iodine studies, including profile scanning, had been performed Since October, 1959, roentgenograms were made of all patients with masses in the thyroid gland, including patients in the wards and clinics of the Mount Sinai Hospital, regardless of whether or not operation was contemplated

Criteria—At the onset of this study we had no definitive criteria for the roentgenological diagnosis of carcinoma of the thyroid [6] In reviewing the films of the first patient with carcinoma in the series, the radiologist (H Z) noted the presence of soft tissue calcifications which were striking in nature and different from those seen on other roentgenograms His report mentioned the possibility of a "new lesion This statement was considered of great importance, since throughout the study he was unaware of the clinical findings and impression The second patient with carcinoma had no definitive roentgenographic findings The film on the third patient showed striking similarities to that of the first, and a diagnosis of carcinoma was tentatively entertained On the basis of the roentgenographic findings in the film of the first and third patients, our criteria were formulated Our fourth patient with cancer showed definite, but minimal, findings and operation was recommended on this basis

Our criteria for malignant lesions, which were identical with those of Holtz and Powers[4] in all essentials, are as follows the appearance of radiopacities of calcifications which are poorly marginated, hazy, not densely calcific, and about equal in size Usually they are grouped in streaks or in a nebular formation within a well-limited area which does not have a calcific rim (fig 1)

In contrast, the calcifications appearing in benign lesions were usually densely calcified, sharply defined, and well marginated, and they varied in size Usually they are haphazardly or individually spaced, but if they are grouped the area most often has a surrounding calcified rim (fig 2)

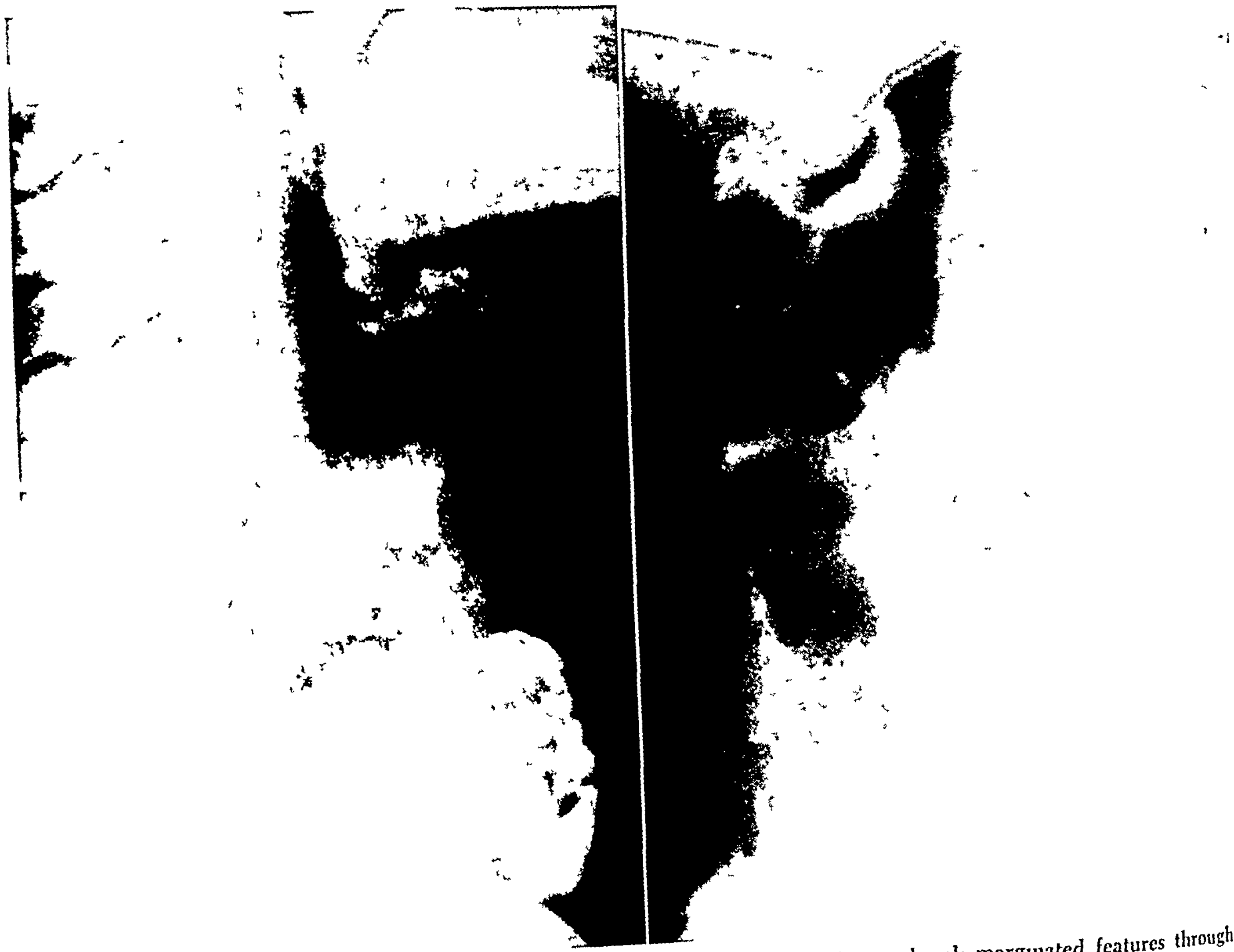

Fig 2 —*Left*, roentgenogram showing unusually large calcific nodule with dense, sharply marginated features throughout, which are seen frequently but are usually much smaller Diagnosis was benign calcification (case 4) *Right*, roentgenogram showing scattered dense calcification, sharply marginated, giving appearance of long duration Diagnosis was benign calcification

A clear differentiation was possible between the calcifications representing the benign and malignant lesions

Results—Roentgenograms were made of 29 patients prior to the primary surgical treatment of their thyroid lesions Six of these proved to have carcinoma of the thyroid, three of whom showed roentgenographic findings diagnostic of thyroid cancer and showed positive results for psammoma bodies on microscopic section Five of these had papillary carcinoma, and in one it was undifferentiated There were no false-positive results in the remaining 23 patients, who represented a variety of benign conditions Table 1 summarizes the clinical and laboratory data on these 29 patients

In addition, 16 other patients were also studied Ten of these had primary cases of thyroid nodules and had not yet been operated upon at the time of this writing All 10 had negative roentgenographic findings Four patients had clinical evidence of local recurrence of a previously treated thyroid cancer, but only one showed positive roentgenographic findings (As yet, however, we have no histological proof of the recurrence in this patient) Roentgenograms of two other patients which were made only after they had received radiation to the thyroid gland for carcinoma, radioactive iodine in one patient and external radiotherapy in addition to radioactive iodine in the other, revealed negative results

Report of Cases

Case 1—A 17-year-old girl had a mass in the right side of her neck in September, 1958 Examination showed the trachea shifted to the left by a nodular right lobe and isthmus Right and left upper jugular nodes were felt Radioactive iodine studies revealed a 47% uptake in 24 hours (normal) and decreased function on the right side At operation a right hemithyroidectomy with excision of the isthmus was performed and the specimen, submitted for frozen section, reported as showing carcinoma A right radical neck dissection, upper superior mediastinal dissection, and left partial neck dissection with left partial thyroidectomy was performed at the same time The final pathology report indicated papillary adenocarcinoma of the right lobe of the thyroid and involvement of nodes in the right side of the neck and superior mediastinum Psammoma bodies were present Thyroiditis was also found in the specimen (fig 1, *left*)

Case 2—A 29-year-old woman had fever associated with pain and tenderness in her neck in 1958 The clinical course and radioactive iodine studies at that time were characteristic of thyroiditis, which subsided after several weeks Five months later a mass was noted in the right lobe of the thyroid The nodule felt cartilaginous and was "cold" on radioactive iodine scanning The clinical diagnosis was carcinoma of the thyroid At operation no involved nodes were felt, and because of suspicious areas in the left lobe a total thyroidectomy was performed The pathology report showed many scattered foci of papillary adenocarcinoma and marked fibrosis Psammoma bodies were seen in the section (fig 1, *right*)

Case 3—A 35-year-old woman had an infected first right brachial cleft cyst On examination, a firm nodular right lobe and isthmus were also noted The patient knew nothing of this and had no symptoms referable to the thyroid gland Twenty-four hour uptake of radioactive iodine was 37% (normal) Profile studies showed equal distribution in both lobes A tentative diagnosis of benign adenomata or thyroiditis was made Roentgenographic studies were performed and indicated the possibility that the patient had carcinoma Operation was urged on the basis of these findings At operation, frozen section of the right lobe showed carcinoma, and a total thyroidectomy and a right radical neck and superior mediastinal dissection was made The patient was reported to have papillary adenocarcinoma of the thyroid and multiple node involvement

Case 4—A 56 year-old woman had a mass in the neck of several years duration Some pressure symptoms were noted Three months prior to her examination the mass had increased in size A stony 3 by-5-cm mass was felt in the right lobe of the thyroid with other nodules in the rest of the gland No nodules were felt On profile study the mass was cold Carcinoma could not be excluded on the basis of the clinical findings Roentgenographic studies of the thyroid were negative for carcinoma At operation, a calcified adenoma in a multinodular gland was found and a subtotal thyroidectomy was performed Pathology report showed multiple adenomas, some with calcification No carcinoma was noted No psammoma bodies were seen (fig 2 *left*)

Comment

Many attempts at the roentgenographic diagnosis of carcinoma of the thyroid have been made in the past Ritvo[7] attempted to use tracheal deviation as a diagnostic sign The subsequent work of Schein, Lentino, and Jacobson[8] clearly showed that this method was misleading and not reliable In patients with advanced disease, in whom resection of the primary lesion may not be feasible, a roentgenographic diagnosis of carcinoma of the thyroid can sometimes be made because of the alteration of the tracheal air space by carcinomatous invasion of the tracheal wall This finding is extremely rare, and in such cases the diagnosis would most likely be evident without the aid of roentgenograms

Table 1—*Summary of Data in Twenty nine Patients Studied by Soft Tissue Roentgenography Prior to Thyroid Surgery*

Clinical Diagnosis	Profile Studies (Radioactive Iodine)*	Soft Tissue Radiography	Pathological Diagnosis
Carcinoma	—	+	Papillary carcinoma
	—	—	Papillary carcinoma
	—	+	Papillary carcinoma
	—	—	Adenocarcinoma
	—	—	Papillary carcinoma
Questionable	—	—	Colloid adenoma
	—	—	Adenoma
		—	Chronic thyroiditis
		—	Chronic thyroiditis
Adenoma	—	—	Calcified adenoma
	—	—	Adenoma
Benign	—	—	Adenoma
	+	—	Colloid adenoma
	—	—	Benign adenoma
	—	—	Adenoma
		—	Benign adenoma
		—	Benign adenoma
	—	—	Chronic thyroiditis
Goiter			
Multinodular		—	Chronic thyroiditis
		—	Adenoma
	—	—	Chronic thyroiditis
		—	Adenoma
Colloid	+	—	Colloid adenoma
Questionable malignancy	—	—	Benign adenoma
	—	—	Chronic thyroiditis
Toxic nodule	+	—	Benign adenoma
Cyst	—	—	Adenoma
Questionable thyroiditis	—	+	Papillary carcinoma
Hyperthyroidism	+	—	

* Plus sign (+) represents hot nodule on radioactive iodine profile studies and minus sign (—) represents cold nodule or no increase in function over nodule in question

The calcifications which are found in thyroid cancer on roentgenographic examination are presumably due to the presence of psammoma bodies in the thyroid A psammoma body is a roughly spherical, laminated body, formed by an acid mucopolysaccharide which binds calcium and iron, among other substances Psammoma bodies are found on histological sections in about 50% of carcinomas of the thyroid gland They are extremely rare in benign lesions of the thyroid The incidence of psammoma bodies in the various types of carcinoma of the thyroid is charted in table 2 These bodies are also sometimes found in nodes having metastatic carcinoma of the thyroid[9] In all patients who showed positive results on roentgenograms pathological slides were positive for psammoma bodies None of the patients with thyroid carcinoma and with roentgenograms showing negative results showed psammoma bodies in microscopic sections Roentgenographic calcium filtration studies to delineate more accurately the nature of the radiopacities seen on roentgenograms may soon be feasible

In anaplastic or small-cell carcinoma of the thyroid the clinical diagnosis is often quite simple because of *invasion of the* surrounding tissues In the follicular and papillary types of carcinoma, early diagnosis may be difficult or impossible With the use of all techniques, including history, physical examination, and radioactive iodine studies, the decision as to the need for surgery still rests upon the clinical judgment of the physician in charge, since, at this time, a positive diagnosis cannot be made on the basis of available techniques The debate as to the advisability of surgery in patients with nodular goiter arises because of the inability to be sure, prior to surgery, that carcinoma is not present [10] The incidence of carcinoma occurring in thyroid nodules has been reported in different surgical series as varying between 4 and 33% [11] It has been calculated that there are 6 million people in the United States with nodules in their thyroid gland Obviously there must be some selection of patients who are to be subjected to surgery. The mortality, if all patients with nodules in their thyroid glands were operated on, would probably far outweigh the possible benefits derived from the early detection of the limited number of thyroid carcinomas that would be found

TABLE 2 —*Incidence of Psammoma Bodies in Various Types of Thyroid Carcinoma**

	Thyroid Tumors		Tumors Containing Psammoma Bodies	
Type of Carcinoma	No	%	No	%
Papillary	303	63	186	61
Follicular	121	25	32	26
Undifferentiated	46	10	6	13
Unclassified	3	2	3	100
Total	473	100	227	48

* Data from Klinck and Winship [9]

Positive results with the use of this roentgenographic technique probably depend on the presence of psammoma bodies As we have noted above, these bodies are found in a great number of patients with papillary and follicular carcinoma of the thyroid In dealing with patients with nodules of the thyroid, either solitary or multiple, we obtain roentgenograms of the thyroid as part of a diagnostic examination Positive results shown on roentgenograms are regarded as an unequivocal indication for operation regardless of radioactive iodine or other studies If a negative result is obtained and if, in our clinical judgement, the thyroid nodule is suggestive of carcinoma and the clinical risks of surgery are warranted, surgery is performed Negative results on roentgenograms are thus not a deterrent to surgery Finally, we have recently used this study as an additional diagnostic aid in an attempt to determine the primary site in a patient who comes to us with metastatic carcinoma from an unknown primary The site of origin is often the thyroid gland, even when a nodule is not palpable Demonstration of this fact in a given patient would then enable the physician to institute a definitive course of therapy which might prolong the patient's life for many years

Summary

Roentgenograms of three of six patients with carcinoma of the thyroid showed positive results according to our criteria No false-positive results were encountered in this series, which also included a variety of benign lesions of the thyroid These findings are presumably due to the presence of psammoma bodies

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Radioactive Iodine Concentration in the Fetal Human Thyroid Gland from Fall-out

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A study was made of the occurrence of I^{131} in human fetal thyroid glands apparently resulting from I^{131} received by the mother from nuclear weapons testing or other types of population contamination. Radioactivity compatible with I^{131} was found in the human fetal thyroid gland. The maximum concentration of I^{131} was 265 μμc per gram of fetal thyroid tissue, 29.1 μμc per gram of adult hog thyroid tissue, and 22.9 μμc per gram of adult thyroid tissue. The highest activity found on a reagent blank was 10.0 μμc. The calculated maximum total radiation delivered to any human fetal thyroid gland was 0.47 rads. The average total dose was 0.05 rads. Extrapolations from data on animals suggest that it is unlikely that this quantity of radiation would produce hypothyroidism or carcinoma of the thyroid gland.

Radioactive iodine, I^{131}, from nuclear weapons testing has been reported to be present in the thyroid glands of adult cattle, swine and sheep, in the fetuses of these sheep, and in adult human beings.[1] Since I^{131} passing from the human maternal to the fetal circulation will be concentrated by the fetal thyroid gland as early as the third month of gestation,[2] we should expect the presence of I^{131} in human fetal thyroid glands. This activity results from I^{131} received by the mother from nuclear weapons testing or other types of population contamination. We wish to report on an investigation we have made of the concentration of I^{131} found in human fetal thyroid glands. The concentration of I^{131} was apparently insufficient to cause hypothyroidism or thyroid carcinoma.

Method

Sources of Specimens.—Twenty-seven human fetal thyroid glands from 25 pregnancies were obtained at the time of abortion, caesarean section, premature labor, stillbirth, or neonatal death during the period Nov. 12, 1958, to Aug. 1, 1959, from four hospitals within a radius of 10 miles of Ann Arbor, Mich.

Only fetuses aged 5 months through term stillbirth (except for one newborn infant, 3 weeks of age) were used in this study. Twelve human adult thyroid glands, not from mothers of these fetuses, were also collected from autopsies at University Hospital Nov. 19, 1958, through March 31, 1959, and analyzed. In addition, 25 adult and fetal hog thyroid glands were collected during the period Jan. 6, 1959, to July 8, 1959, from a local abattoir and used as controls. These hogs were all from Washtenaw County (around Ann Arbor, Mich.).

Data on age of fetuses, causes of death, condition of fetus, history of maternal systemic disease, maternal thyroid or iodide medication, or maternal thyroid disease were obtained at autopsy on the fetus, by examination of the medical records of the mother, and by interview of the mother. These data are presented in the table.

Preliminary Treatment of Thyroid Glands.—Most thyroid glands used in this study were dissected free of the fetus by the pathologist within one hour after delivery of the fetus. Histologic sections were obtained on many thyroid gland specimens to identify the tissue as thyroid gland. None of the sections showed a significant degree of autolysis. If chemical extraction of iodine from the thyroid tissue had to be delayed, the tissue was immediately frozen and stored at approximately −40° C until the time of analysis. The chemical extraction was always begun within a period of one hour to three days after delivery of the fetus.

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Care of Apparatus—All apparatus and instruments used for analyses of human and hog thyroids in these experiments were stored and used separately from all other equipment in our laboratory A second complete set of apparatus was used for recovery experiments It was never used for unknowns At the beginning of this study, pipettes were not isolated as described above, but in the latter part of the study separate sets of pipettes were also maintained for each type of experiment

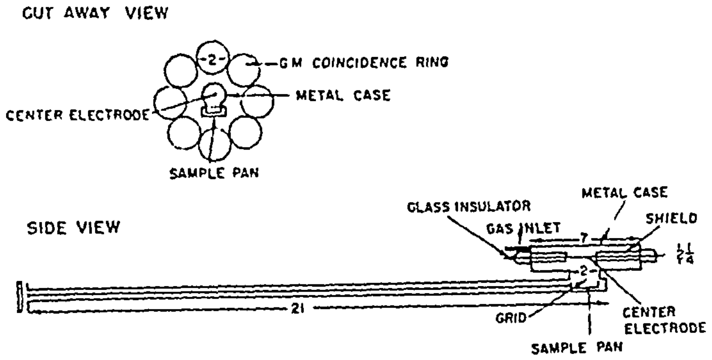

Fig 1 —Diagram showing assembly of low-background G-M counter in which filter papers were counted

Chemical Extraction of I^{131} from Thyroid Tissue—Chemical extraction of I^{131} from thyroid tissue consisted basically of four steps mechanical preparation of the tissue, digestion with oxidizing agents, distillation of the I^{131} out of the digest, and drying of the collected distillates Fresh thyroid tissue was dissected free of fat and weighed If the thyroid tissue weighed less than 1 Gm, normal rabbit serum was added to supplement the protein content to a total weight of 200 mg (the estimated amount of protein in 1 Gm of thyroid tissue) The tissue was minced and transferred to a digestion flask containing, in analyses of hog thyroids, 3 5 ml and in all other experiments 2 5 ml of chromic acid reagent, 40 0 ml of sulfuric digestion reagents and glass beads[3] Parts two and three of the Hycel Hormone Chemical Company's modification of the original Barker method[4] were followed, as described in their procedure manual[3] with the following two modifications At the suggestion of Dr Barker,[5] the distillate was collected in a trap solution containing 0 1 N sodium arsenite in 20% sodium hydroxide rather than into a solution of sodium hydroxide alone No arsenious acid reagent was added to the centrifuge tube into which the distillate was drained

The distillate was poured into a micro-buret and dripped slowly onto filter paper disks measuring 22 mm in diameter The disks were supported between slits in two waxed paper cups and a stream of warm air was used to facilitate drying

Reagent Blanks—Eleven reagent blanks were prepared and counted during the period from Nov 30, 1958, through July 28, 1959 Three milliliters of stored normal rabbit serum, 2 5 ml of chromic acid reagent, and 40 0 ml of sulfuric digestion mixture made up the reagent blank Digestion and distillation were carried out as described above

Recoveries—In order to test recovery, six additional experiments using 0 03 to 0 2 μc of I^{131} in the form of added carrier-free NaI^{131} or in the form of I^{131} already incorporated into thyroid tissue were carried out The mean over-all recovery was 73 6% ± 6 2 (standard deviation) Counts made at various stages of the procedure showed that most of the loss occurred during drying on the filter paper

Counting of Samples—The filter papers containing the dried distillate were counted side by side in a windowless gas-flow Geiger counter surrounded by an anticoincidence ring of G-M (Geiger-Muller) counters 61 cm in length and 5 7 cm in diameter The counting assembly was housed in a cave of old iron bricks with a minimum thickness of 8 in A diagram of this assembly is seen in figure 1

The background count in the counting chamber not canceled by coincidence counts from the ring of Geiger counters was approximately 1 6 counts per minute

Each sample was counted for four hours or more and background counts were run overnight Since the counts occurring in the counting chamber not canceled by a simultaneous pulse from the coincidence ring increased proportionally with an increase in the counts canceled by the coincidence ring, all uncanceled counts were standardized to a canceled count of 25 counts per minute, an average value Samples showing activity greater than twice the background count were recounted weekly until the fall in count rate showed a plateau

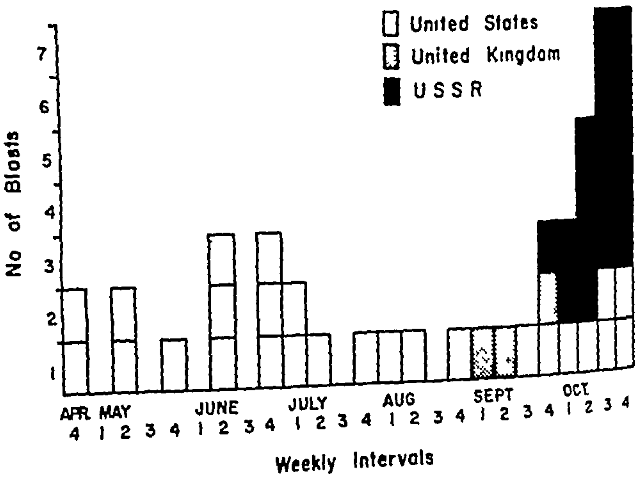

Fig 2 —Frequency of atomic blasts in 1958

A line of best fit was calculated from the data, assuming a single isotope decay rate From this line the half-life of the radioisotope counted was determined Because the half-lives thus determined agreed closely with the half-life of I^{131}, the activity of each sample was calculated back to the day of fetal delivery, using the decay rate of I^{131}

The over-all efficiency of the counting system was found by drying a known volume of a solution of I^{131} containing a known number of disintegra tions per second on filter paper, as described above. This standard was then counted in the usual manner. The over-all efficiency of the counting system was thus found to be 14%. This value included the loss of activity during the drying process, about 26%. With this knowledge the number of micromicrocuries of I^{131} per gram of fetal thyroid tissue and per total thyroid gland was calculated.

Results

Nuclear Weapons Testing.—Figure 2 is a bar graph presenting the frequency of nuclear blasts during 1958 by the United States, Great Britain, and Russia.[6]

A maximum atmospheric concentration of I^{131} would be expected to occur during the last week of October. Our sampling began less than two physical half-lives after the last blasts. We have not been informed of the occurrence of any further nuclear weapons testing during the period of November, 1958, to August, 1959.

Data on Human Fetuses and Their Mothers.—The table presents data on human fetuses and their mothers. Repeated counting of extracted material from seven fetal thyroid glands collected over the period Nov. 24, 1958, through May 12, 1959, gave values of radioactive half-life ranging from 7.5 to 9.8 days and averaging 8.4 days, roughly the half-life of radioactive iodine, I^{131} (8.1 days).

Although the median I^{131} content of the reagent blanks was equivalent to only 2.1 μμc, the maximum I^{131} content was equivalent to 10.0 μμc. This maximum is higher than the fetal thyroid gland I^{131} concentration of all but eight fetuses. Excluding the dates Nov. 30, 1958, to Dec. 23, 1958, however, the activity of reagent blanks never exceeded 3.5 μμc per gram. Only two human fetal thyroid glands were obtained during the above interval. Excluding these two fetal thyroid glands, only eight fetal thyroid glands failed to exceed the maximum reagent blank activity of 3.5 μμc. These eight glands are scattered fairly uniformly throughout the period Feb. 27, 1959, to July 24, 1959.

Figure 3 presents a comparison of the concentration of I^{131} in the human fetal thyroid gland to the concentration in human adult and hog thyroid glands, and in reagent blanks during the same period of sampling.

It is important to note that the plot in figure 3 on a semilog scale minimizes the apparent fetal thyroid gland peak concentrations of I^{131} and tends to emphasize small variations in activity in samples containing little activity. The following observations from figure 3 are noteworthy.

1. These four groups of samples may be listed in order of average decreasing concentration of radioactivity as follows: fetal thyroid gland, hog thyroid gland, human adult thyroid gland and reagent blanks. Generally, the fetal thyroid I^{131} concentration is 2 to 10 times greater than the human adult thyroid I^{131} concentration and shows greater variation. One group of pooled hog fetal thyroids showed a 58% greater concentration of I^{131} than was found in the mother's thyroid.

It is of interest that the twin human fetuses 13 and 14 showed only a 9% difference and twin fetuses 25 and 26 showed only a 39% difference in concentration of I^{131}. The total thyroid gland I^{131} content of the twins in each instance was roughly the same, even though the concentration of I^{131} differed.

2. Fetal thyroid gland I^{131} concentration decreased during the period December, 1958, through March, 1959, with an apparent half-life of about 20 days.

3. The variation in concentration of I^{131} from one fetal thyroid gland to the next is roughly tenfold to twentyfold during the period from November to February. The variation in concentration then appears to become less as the concentration in all specimens falls between February and May.

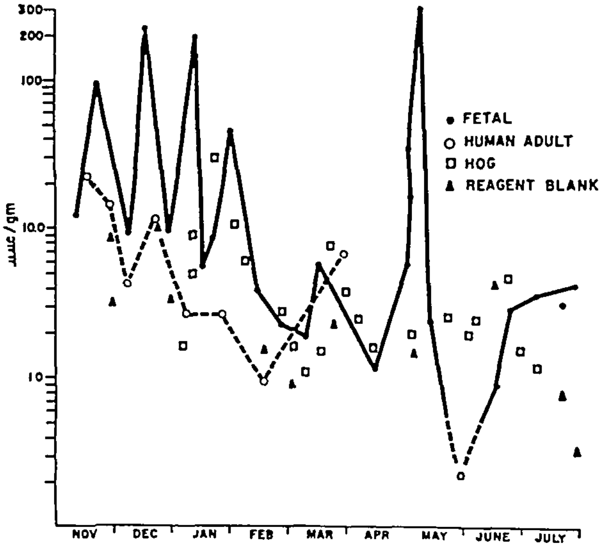

Fig. 3.—Comparison, by month, of concentration of I^{131} in thyroid gland specimens and in reagent blanks.

4. The concentration in fetal thyroid gland specimens in May builds up progressively through four successive specimens to a peak hundredfold increase, with no similar rise in hog thyroid gland or reagent blank I^{131} concentration.

I^{131} Content and Fetal Age.—Histological study of human fetal thyroid tissues demonstrated that colloid-containing follicles were clearly evident in all specimens past 4 months of fetal age. Our data suggest that the fetal thyroid gland weight increases until 7 months of age and then reaches a plateau. No correlation is apparent between I^{131} concentration in the human fetal thyroid and age of the fetus or weight of the thyroid gland after the fourth month of gestation.

Correlation of I^{131} Content of Fetal Thyroid with Condition of Fetus and Thyroid Status of Mother.—No relation was observed between the cause of death in the fetus and the I^{131} concentration of the thyroid gland. Fetus 4, with the second highest concentration of I^{131} in his thyroid gland, died at

6 months of age after premature birth with cerebral agenesis and possible hyaline membrane disease Fetus 7, with one of the lower concentrations of I^{131} in thyroid tissue, died after a full-term birth with hydrocephaly and a meningocele

The mothers of fetuses 3 and 7 had taken desiccated thyroid during pregnancy The mother of fetus 20 had been given compounds containing organic iodine, and the mother of fetus 24 had had inorganic iodine during pregnancy All of these fetuses had low concentrations of I^{131} in their thyroid glands, in spite of the fact that the thyroid glands of fetuses 3 and 7 were collected at the time when the concentration of I^{131} in thyroid gland specimens was running high There is insufficient data, however, to allow one to conclude that medicament containing iodine ingested by the mother or injected into the mother during pregnancy decreased the I^{131} concentration in fetal thyroid gland

Calculated Irradiation Dose Delivered to Human Fetal Thyroid Gland—Certain assumptions are made in calculating the dose of radiation in rads delivered to fetal thyroid glands These assumptions are that all beta radiation from thyroid I^{131} was absorbed in fetal thyroid tissue, that radiation from gamma rays may be ignored, that, as in fetal sheep,[1c] the concentration of I^{131} in fetal thyroid tissue rises exponentially from day 50 to 150 and then remains constant with a constant intake of I^{131}, and that no decreased concentration of I^{131} in human fetal thyroid gland resulted from irradiation of the fetal thyroid gland We are aware of the fact that the I^{131} intake from fall-out is not constant, that we do not know the concentration of fetal thyroid I^{131} during the actual period of weapons testing, and that calculation of the dose with use of these assumptions does no more than set an upper limit to fetal thyroidal I^{131} under the specific conditions of our study

First, in order to calculate the maximum possible absorbed dose to a fetal thyroid gland we assumed that the intake of once-labeled diet throughout the gestation period was constant at a level which resulted in the maximum observed concentration of 265 $\mu\mu c$/per gram Two formulas must be used, one to calculate the cumulative dose during the initial period of exponential increase in I^{131} concentration, the second to calculate the cumulative dose after the concentration of I^{131} reaches a plateau The dose to the thyroid gland during the initial period from 50 to 150 days is given by the equation, $D\beta = 73 8 \times \bar{E} \times C_o \times T(½) \times [1 - \exp(\frac{0 693 t}{T(½)})]$,

where $D\beta$ = absorbed beta dose in rads,

$\bar{E}\beta$ = average energy of the beta particle disintegration in mev,

C_o = concentration of the isotope in microcuries per gram of thyroid tissue,

t = time of exposure in days, and

$T(½)$ = doubling period of the I^{131} concentration in days

Substituting into the formula we have $D\beta = 73 8 \times 0 19 \times 2 65 \times 10^{4} \times 20 \times [- \exp(\frac{-0 693 \times 100}{20})]$, so that $D\beta = 0 04$ rads to the thyroid between 50 and 150 days

Data on Human Fetus

Fetuses, No	Delivery Date of Specimen	Weight of Fetal Thyroid Specimen Obtained Gm	Estimated Amount of Whole Thyroid Gland Lobes	First Count Obtained Cpm	Interval Between First Count and Delivery Date Days	Activity in Disintegrations Per Minute	Physical Half Life of Isotope Days
1	11/12/58	0 38	½	0 1	31	0 7	Cannot be calculated
2	11/24/58	0 18	½	3 1	6	22 6	7 9
3	12/10/58	0 77	2	1 3	6	9 5	Cannot be calculated
4	12/19/58	0 28	2	11 9	5	80 9	9 1
5	1/ 1/59	0 02	2	1 3	4	9 5	8 4
6	1/14/59	0 39	1	16 0	4	117 0	7 6
7	1/17/59	1 06	1	1 2	5	8 5	Cannot be calculated
8	1/22/59	0 37	1½	0 6	5	4 6	
9	2/ 2/59	0 48	2	6 4	2	39 6	7 5
10	2/15/59	0 66	1 3/5	0 5	3	3 9	
11	2/27/59	0 37	1 3/4	0 2	4	1 3	
12	3/10/59	0 37	2	0 2	3	1 2	
13 twins	3/17/59	0 40	2	0 5	3	3 4	
14	3/17/59	0 54	2	0 6	3	4 3	
15	4/16/59	1 01	1 4/5	0 3	2	2 1	
16	5/ 4/59	0 36	1	0 5	3	3 3	
17	5/ 5/59	0 41	½	3 1	3	22 5	
18	5/ 5/59	0 63	2	1 9	5	13 8	8 6
19	5/12/59	0 55	2	34 6	3	253 0	9 8
20	5/14/59	0 61	1	0 3	4	2 1	
21	6/ 1/59	0 43	1½		1		
22	6/19/59	1 05	2	0 2	4	1 4	
23	6/25/59	0 59	2	0 3	4	2 4	
24	7/ 9/59	0 95 used 1 43 total	2	0 5	7	3 8	
25 twins	7/20/59	0 44	2	0 3	3	2 0	
26	7/20/59	0 26	2	0 3	4	1 8	
27	7/28/59	0 07	1½	0 1	6	0 4	

* Values were rounded to significant figures after calculations were performed

The second formula, $D\beta = 51\ 2 \times \bar{E}\beta \times C_0 \times t$ expresses the absorbed dose between 150 and 270 days where the symbols are the same as above

Then $D\beta = 51\ 2 \times 0\ 19 \times 265 \times 10^{\ 4} \times 120$ and $D\beta = 0\ 31$ rads to the thyroid between 150 and 270 days Adding 0 04 rads delivered during the initial build up period to the subsequent 0 31 rads accumulated during the last 120 days of intrauterine life, the calculated maximum cumulative dose to any fetal thyroid in our series is 0 35 rads Correcting this for a chemical recovery of 74% the dose becomes 0 47 rads

A second calculation, the mean observed exposure dose, was performed with the data used to obtain a more realistic figure The mean observed exposure dose we took to be the dose in rads to a fetal thyroid if the gestation period corresponded to the nine-month period of our study and the concentration of I^{131} in the gland varied as shown by our values This calculated dose was obtained by averaging the fetal thyroid I^{131} concentrations gravimetrically, then applying the preceding equations The total corrected dose obtained was 0 05 rads

*es and Their Mothers**

I^{131} Content of Fetal Thyroid Gland at Delivery		Age of Fetus Mo	Condition of Fetus	Remarks About Mother
μμc/Gm	μμc/Thyroid Gland			
12 0	18	7	Died 10 days after premature birth	
94 4	68	6½	Caesarean section because of diabetes with complications	No information
9 2	7	6	Stillborn macerated fetus	Taking thyroid pills
216 0	60	6	Neonatal death cerebral agenesis hyaline membrane disease	
9 6	6	9		
189 0	148	8½	Lived 12 hr hyaline membrane disease	No history
5 5	12	9	Neonatal death due to hydrocephalus meningocele	On thyroid previous thyroidectomy
8 5	4	6¼		History noncontributory
44 5	21	9		
3 7	3	9	Rh incompatability lived 4 hr	History noncontributory
2 2	1	9	Stillborn term	History noncontributory
1 8	1	5½		Fourth pregnancy lost
5 4	2	6½	Asphyxia abruptio placenta	History noncontributory
5 1	3	6¼	Same twins	
1 1	1	9	Amniotitis	
6 3	4	6	Persistent fetal atelectasis prematurity	
31 7	52	9	Persistent fetal atelectasis died 48 hr after delivery	History noncontributory
15 0	10	9	Stillborn	
265 0	147	9	Anoxia intrauterine death cord prolapse	History noncontributory
2 2	3	9	Intrauterine death	
		7½	Premature labor neonatal death	Endometritis IV pyelogram
1 8	1	9	Death within 24 hr of delivery cord about neck aspiration of amniotic fluid	History noncontributory
2 6	2	9¾	Polycystic kidney and hydroureter	History noncontributory
3 3	5	9	Hydrops fetalis	Took cough medicine for 2 days
2 7	1	9		History noncontributory
4 4	1	9		History noncontributory
3 8	0 4	5	Premature infant dead on arrival in emergency	History noncontributory arrested pulm tbc

Comment

Radioactivity in Reagent Blanks—As the activity in reagent blanks was not sufficient to identify I^{131} by repeated countings, we have no proof that the radioactivity is from I^{131} For purposes of comparison, however, it was assumed that the counts were from I^{131} and activity was extrapolated to zero time and converted to micromicrocuries

As the activity in reagent blanks roughly paralleled (at a lower level) the I^{131} concentration in thyroid tissue, it is reasonable to assume that the activity came from air fall-out into reagent bottles or from fall-out I^{131} entering the blood stream of the rabbit from which the carrier serum protein was obtained Carrier protein was added to reagent blanks and to other samples with insufficient amounts of tissue protein, because recoveries have been found [4] to be lowered when insufficient protein is present initially

Identification of I^{131} as the Source of Radioactivity—The identification of I^{131} as the source of the majority of the radioactivity in the samples of thyroid glands by the technique of radioactivity half-life determination did not furnish unequivocal proof that I^{131} was the major source of radioactivity in these samples At least seven other radioisotopes have similar half-lives Only Ag^{111} (radioactive silver) and Sn^{125} (radioactive tin) are products of fission As neither of these isotopes are concentrated by the thyroid gland similar to I^{131} (half-life = 8 1 days), it is unlikely that any radioisotope other than I^{131} accounts for the radioactivity found in our thyroid gland samples Moreover, the radioactivity material finally counted had first been isolated from the thyroid tissue by a multi-step chemical procedure specifically designed to isolate and recover iodine

Relative Radioactivity of Four Groups of Samples—Extrapolating from studies in fetal sheep and cattle, the human fetal thyroid gland would be expected to show a higher concentration of I^{131} than the human mothers thyroid gland during the third trimester Barnes and colleagues [16] found that the thyroid glands of offspring of dams fed 0 15 μc of

I^{131} per day showed 1.8 to 2.9 times the I^{131} concentration of their mothers' thyroid glands after 130 days of pregnancy. Gorbman and co-workers[7] demonstrated that the concentration of I^{131} was six to seven times greater in the fetal thyroids of cattle than in their mothers' thyroids, although the total content of I^{131} was only twice that of the mother's thyroid gland. Histologically the thyroids of these cattle appeared much less active than those of their fetuses. He believed that a disparity of thyrotropic hormone concentrations in the fetal and maternal circulation was the most reasonable explanation for the disparity in thyroidal function between the mother and its near-term fetus. It is probable that Hodges and colleagues[2b] demonstrated, after tracer doses of I^{131} to mothers, a lower concentration of I^{131} in fetal thyroid than in maternal thyroid glands of human beings, because the fetuses they studied were younger than ours. We are not aware of any other studies demonstrating the relative I^{131} concentration in human fetal thyroid gland in comparison with human adult thyroid gland. It should be stressed, however, that our finding of a concentration of I^{131} in fetal thyroid amounting to 2 to 10 times the concentration in human adult thyroid gland does not necessarily hold strictly for any individual mother and her fetus. Our adult human thyroid glands were not from mothers of the fetuses studied.

Our data showing a concentration of I^{131} in the thyroid glands of swine higher than in the thyroid glands of human adults complement the data of Van Middlesworth. Swine in Memphis showed a thyroid concentration of I^{131} from fall-out 5 to 10 times the concentration in adult human beings in Memphis during 1958.[8]

Fall in Fetal Thyroid Gland I^{131} Concentration After Nuclear Weapons Testing.—Our data show no significant decrease in thyroid gland I^{131} concentration during the first month after cessation of nuclear weapons testing. Van Middlesworth[9] demonstrated that rats fed I^{131}-tagged diets were almost in equilibrium, as judged by the fact that the I^{131} content of their excreta was 90% of the intake, by the 16th day on the tagged diet. Bustad and co-workers[10] feeding adult sheep a constant daily intake of I^{131}, found that the concentration of I^{131} in their thyroid glands reached an initial plateau after 10 to 40 days, with a mean of 17 days.

It is logical to suppose, therefore, that the apparent absence of decrease in fetal I^{131} concentration in the first few weeks after cessation of weapons testing and the apparent subsequent decrease in fetal thyroid I^{131} activity between December, 1958, and March, 1959, with a half-life of approximately 20 days, was also related to the time taken for establishment of I^{131} equilibrium between mother and fetus.

Fetus-to-Fetus Variation in Thyroidal I^{131} Concentration.—We have no good explanation for the tenfold to twentyfold fetus-to-fetus variation in thyroidal I^{131} concentration. Variation of similar magnitude has been observed by others, however, in sheep and man. Bustad and co-workers[10] found a tenfold variation from sheep to sheep on the same day in the same group fed the same diet with a fixed content of I^{131}. Comar and colleagues[1c] found that in May, 1955, 30% of the adult human thyroid gland samples had less than 0.0008 mμc of I^{131} from fall-out per gram, whereas 11% had more than 0.01 mμc per gram, a one-hundred-twenty-five-fold variation. Although all our thyroid gland specimens were from patients and hogs within a 50-mile radius of Ann Arbor, the intake of I^{131} from fall-out is certainly more variable than intake on a regular diet of fixed I^{131} content. The 9% difference in human fetal thyroid I^{131} concentration in one set of twins and the 39% difference in another set of twins, give some idea of the order of magnitude of variation in I^{131} concentration that may be found under ideal conditions. The fact that the total I^{131} content of the thyroid glands of twins differed much less than thyroid glands of unrelated fetuses suggests that variations in weights of the thyroid glands from fetus to fetus might be a factor in these differences. The larger thyroid glands of twin fetuses showed the lowest concentrations of I^{131}.

Peak of Radioactive Concentration in May, 1959.—The peak fetal thyroid I^{131} concentration in May, 1959, is noteworthy. The magnitude of this concentration equals the concentration found during the month after cessation of nuclear weapons testing. We have several reasons for believing that this peak of I^{131} concentration does not represent contamination of specimens with I^{131} in the laboratory. The peak is made up of four fetal thyroid glands delivered and extracted on different dates. Each successive specimen shows a regular and progressive increased concentration over the previous specimen. A reagent blank and a hog thyroid specimen prepared and counted during this same interval do not share this increased I^{131} concentration. Hogs in this area are fed grain kept in drums. Milk from cows on the same farms is mixed with this grain. We were able to find radioactivity in milk but the radioactivity did not have a half-life compatible with I^{131}.

Van Middlesworth[8] demonstrated the presence of increased I^{131} radioactivity in the thyroid glands of Seattle sheep at the end of April and in Seattle cattle in May. Increased concentrations of radioactivity were also observed during May and June by the United States Public Health Service in connection with their 12 milk sampling stations.[11]

In vivo counting over the thyroid gland of the mother of the fetus with the greatest thyroid activity detected no evidence of thyroid radioactivity. She gave no history of having I^{131} for tracer studies or treatment in the past.

If this May peak in fetal thyroid I^{131} concentration was from fall-out, the source of atmospheric contamination apparently was not a nuclear weapons blast.

In spite of these data arguing against laboratory contamination of the fetal thyroid, or I^{131} administered to the mother by her physician, these sources of contamination are still a possibility The very rapid build-up and fall off of activity in these fetal thyroid glands sampled in May are difficult to explain on any other basis

Correlation of I^{131} Content of Fetal Thyroid with Condition of Fetus and Thyroid Status of Mother—It is not surprising that fetus 4, with cerebral agenesis, was able to concentrate I^{131} avidly in his thyroid gland Yamazoki and colleagues[12] have just reported that in two anencephalic fetuses of mothers given tracer doses of I^{131} the thyroid was able to synthesize the normal thyroidal iodine compounds

It is logical to expect that if the mother were given desiccated thyroid during pregnancy her own thyroid gland's accumulation of I^{131} from fall out would be suppressed The average dose of desiccated thyroid to the mother, however, would not be expected to suppress fetal thyroid gland activity[13] unless iodine from the thyroid medication diluted I^{131} in fetal thyroids We have no explanation, therefore, for the fact that the thyroid glands of fetuses 3 and 7 showed relatively low concentrations of I^{131} at a time when other fetuses showed high concentrations

It does seem evident, however, that all fetal and maternal factors which might affect the concentration of I^{131} by the fetal thyroid gland appear to be dwarfed in their significance by variations in the concentration of I^{131} in fall-out

Radioactivity in Human Fetal Thyroid Required to Produce Hypothyroidism—As we have observed no histological changes in the fetal thyroid gland specimens compatible with I^{131}-induced decrease in thyroid function, and as fetuses tested during maximum fall-out concentrations concentrated I^{131} well in their thyroid glands, we have no evidence that even the maximum I^{131} concentration in a fetal thyroid gland observed in this series was sufficient to produce hypothyroidism by the time of counting

Could subtle radiation damage in the fetal thyroid produce hypothyroidism later in life? It is difficult to extrapolate from the few pertinent animal experiments to man

Bustad and colleagues[14] found no evidence of hypothyroidism in the offspring of sheep fed 5μc per day throughout pregnancy and during breast-feeding of these offspring for four months The offspring were then fed 5μc of I^{131} a day for five years and killed The calculated total dose of irradiation received by a representative animal was 30,000 rads for the entire 5 years of life

If any type of extrapolation from these data to our data on the human fetus were justified, it seems unlikely that even the maximum concentration of I^{131} found in human fetal thyroid would have resulted in hypothyroidism

Radioactivity in Human Fetal Thyroid Required to Produce Neoplasm—It is impossible for us to conclude that radiation from I^{131} in our fetal thyroid glands was sufficient to produce neoplasms, as none were observed in our histological sections It is also dangerous to extrapolate from the few pertinent animal experiments to man Bustad and colleagues,[14] observed the development of thyroid adenomas under the conditions stated above from daily I^{131} intake in four of five sheep receiving an estimated total dose of 30,000 rads A metastasizing fibrosarcoma involving the thyroid gland was found in the fifth sheep Six ewes exposed to 0 15 μc per day and 25 nonirradiated controls showed no involvement This dose of irradiation, however, is greatly in excess of the doses observed here and therefore not pertinent to our observations

Summary

Twenty-seven human fetal thyroid glands from 25 pregnancies, 12 human adult thyroid glands, 25 adult and fetal hog thyroid glands, and 11 reagent blanks were analyzed for I^{131} activity from fall-out

Radioactivity compatible with I^{131} was found in the human fetal thyroid gland The maximum concentration of I^{131} was 265 μμc per gram of fetal thyroid tissue, 29 1 μμc per gram of adult hog thyroid tissue, and 22 9 μμc per gram of adult thyroid tissue The highest activity found on a reagent blank was 10 0 μμc Data on fetal pathology, age of fetus, thyroid status of mother during pregnancy, and frequency of nuclear weapons testing have been examined for correlation with the degree of concentration of I^{131} in fetal thyroid

The calculated maximum total radiation delivered to any fetal thyroid gland was 0 47 rads The average total dose was 0 05 rads Extrapolations from others data from animals suggest that it is unlikely that this quantity of radiation would produce hypothyroidism or carcinoma of the thyroid gland

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George E Bowler, D V M and Carl Wetzel, manager of the Ann Arbor division of the Peter's Sausage Co , provided the fetal hog glands used in this study

Miss Patricia Dahlstrom carried out all counting measurements used in this study Katherine Elzinga, Jean Cofell, and Sharon Owings participated in the chemical extraction of I^{131} from thyroid tissue

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Cardiotoxic Thyroid and Radioactive Iodine

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A study was made of 43 patients with heart disease who could not be restored to a comfortable state of ambulation by treatment with digitalis, diuretics, low-sodium diet, and other medication In this group there were 5 men and 20 women with definite evidence of thyroid abnormalities In none of the 25 was the hyperthyroidism diagnosed clinically, although it was looked for by both history and physical examination, the evidence was obtained in each case by the radioactive iodine (I^{131}) tracer technique The diagnostic and therapeutic use of I^{131} is exemplified in the history of a 53-year-old man with angina pectoris It is believed that by careful adjustment of I^{131} dosage the patient can be brought to a state of normal rather than subnormal thyroid function The procedure outlined gave marked improvement in all patients but two who died of myocardial infarction

Thyroid disease can usually be diagnosed clinically, even when there is minimal evidence of thyrotoxicosis and the thyroid is not palpable It is accepted that this diagnosis frequently calls for effort and attention on the part of the clinician, and occasionally the diagnosis is elusive even with the most experienced Diagnostic skills in recent years have been supplemented by laboratory procedures that have made it possible for the clinician to verify an opinion and institute proper therapy in the presence of thyroid disease that affects the heart

In the early 1930's many papers were published[1] that advocated total thyroidectomy as a treatment for heart disease This procedure did not meet with universal enthusiasm from physicians and was eventually dropped as a subject in the literature Somewhat later, in the early 1950's, radioactive iodine (I^{131}) was used in the treatment of heart disease, the rationale for this procedure was similar to that used earlier by those who had advocated surgical removal of the thyroid gland Two large series of cases were reported in 1955,[2] one of 1,070 and one of 231 cases These two series included 814 cases of angina pectoris, 428 cases of congestive heart failure, and 59 cases of combined congestive heart failure, and 59 cases of combined congestive

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From the Department of Medical Physics, William Beaumont Hospital, Royal Oak, Mich heart failure and angina pectoris Radioactive iodine was prescribed, usually in divided doses of 5 or 6 mc until a total dose of 30 to 50 mc was reached and hypothyroidism was produced clinically Improvement was noted in from 60 to 93% of these cases

Obliteration of the thyroid gland, then, has been reported to have caused improvement in patients with heart disease in which there was no clinical or pathological evidence of thyroid abnormality The surgical pathology of the thyroid was reviewed by Hertzler in a monograph published in 1936 [3] In this monograph he warned that when improvement occurred in cases of heart disease after total thyroidectomy, it was probably because an abnormal thyroid gland had been removed

There is evidence now [4] that there is a form of pure thyroid heart disease that is not related to the presence of coexisting heart disease of any other type It is recognized [5] that the thyroid may have more than one secretion and that its products are abnormal in at least some disease states [6] Coupled with this slowly growing body of information about thyroid function is the knowledge that myxedema or total absence of thyroid function also causes abnormalities of the heart and circulation [7] This somewhat incompatible set of circumstances leads to the thought that when there has been improvement in a patient with heart disease as the result of the removal of the thyroid gland, by any method, it is possible that the gland was abnormal initially

Clinical Material and Methods

With the knowledge that it is possible to detect abnormalities of thyroid function, both concealed and otherwise, by I^{131} tracer techniques,[8] it was decided in December, 1956, to proceed with tracer studies in all patients with heart disease that responded poorly to treatment and in which a diagnosis of thyroid disease could not be made clinically Poor response was defined broadly as the inability to reach a comfortable state of ambulation with the usual therapy, i e, digitalization, administration of diuretics, low-sodium diet, and medication Through Jan 31, 1959, there were 43 such cases Of these 25, or 58%, revealed definite evidence of thyroid abnormalities (see table)

Five patients were men and 20 were women The age range in women was from 32 to 75 years and in men was from 48 to 64 years The thyroid was palpable and nodular in 10 of the reported cases, and five patients had had operations on their thyroid glands 10 or more years ago In none of these 25 cases was hyperthyroidism diagnosed clinically, although it was looked for by both history and physical examination Elevated intrinsic thyroid function was found in each of these 25 cases reported by I^{131} tracer technique These hyperfunctioning thyroid glands were reduced to normal functioning tissue by controlled treatment with I^{131} The technique of therapy and follow-up examination calculated to produce normally functioning thyroid glands and not hypothyroidism is illustrated by the following case report

Report of a Case

Case 18 —A 53-year-old man with angina pectoris is typical of patients in the series and will illustrate the procedures used in this study This patient had angina of effort for two years prior to the first tracer study His angina was becoming increasingly severe, more frequent, and less promptly relieved by administration of nitroglycerin He worked as a newspaper distributor and was required to do considerable lifting and walking in his occupation In spite of treatment with the usual dietary and other standard medical approaches, he was becoming increasingly disabled, and at the time of the first I^{131} tracer study was not able to work at all Physical examination remained essentially noncontributory during the first two years of observation Blood pressure was recorded at levels of about 140/80 mm Hg and the heart showed regular sinus rhythm with a resting rate of about 84 per minute There were no murmurs heard over the heart, and the chest was always found to be normal on physical examination The spleen and liver were not palpable, and the abdomen was considered normal

The central nervous system did not present any localizing findings, and the clinical and family histories were noncontributory There was no history of diarrhea or bouts of irregular heart rate that could be considered evidence of hyperthyroidism Laboratory studies from time to time, including roentgenograms of the chest, gallbladder visualizations, and complete gastrointestinal series, were all within normal limits Electrocardiograms in series were normal Blood chemistry studies included determinations of blood urea nitrogen, fasting blood sugar, and blood cholesterol contents, which were found to be within normal limits The patient's basal metabolic rate at this time was +10% A protein-bound iodine study was not done This patient had angina pectoris relieved by administration of nitroglycerin, without any immediate evidence of other disease It was decided that he be included in this series of cases, and as a result his thyroid function was studied by I^{131} tracer technique

In each of these cases a complete tracer study was performed This included a measurement of the percentage concentration of the tracer at the end of 24 hours, and many of these were within normal limits In addition a sequence of studies was performed with use of a Geiger-Mueller counter directly in contact with the surface of the skin In hospitalized patients the sequence was five complete studies in 32 hours, in the ambulant patients the study was performed at the end of 2 and of 24 hours The size, shape, and position of the gland was outlined, and a search was made for any aberrant localizations or extensions The sequence of counts made it possible to evaluate abnormal rate of gain or loss of the tracer The presence of any abnormality in the gland, whether hyperfunctioning or hypofunctioning foci, was determined. In most of the cases reported, adenomatous foci were demonstrated by the contact counting. In these the size, location, and intrinsic function of the focus was recorded in detail. This is the standard procedure routinely used for localization of toxic adenomas prior to surgery and has been used suc

Data on Twenty-five Patients with Heart Disease Showing Thyroid Abnormality

Case No	Date	Age Yr	Sex	Manifestation of Heart Disease	Thyroid	Original Results of I^{131} Tracer Studies	I^{131} Treatment		Follow up Tracers Date	Clinical Improvement, %	Thyroid Function After Treatment
							Date	Amount Mc			
1	12/15/56	68	F	Heart failure	Not palpable	32% concentration 2 cm area 3 times normal function	12/20/56 12/28/56	5.5 5.5	4/ 4/57	90	34% concentration no intrinsic elevation
2	12/28/56	75	F	Angina pectoris	Not palpable	38% concentration, 3 cm area, twice normal function	1/ 4/57 1/11/57 11/ 8/57	4.0 3.8 6.0	3/22/57 6/13/57 11/ 7/57	75	33% concentration no intrinsic elevation
3	1/ 7/57	66	F	Heart failure	Small palpable and nodular	67% concentration nodular area 4 times normal function	1/ 8/57 1/11/57 5/13/57 8/ 5/57 8/ 9/57 10/30/57 11/ 5/57 11/15/57	3.8 4.2 2.3 4.0 4.0 4.0 4.0 4.0	5/13/57 7/27/57 10/28/57 5/15/58	80	30% concentration no intrinsic elevation
4	1/29/57	55	F	Sinus tachycardia	Not palpable	19% concentration discrete foci, 3 times normal	2/ 1/57 2/12/57	4.0 4.0	5/ 2/58 9/16/58	100	41% concentration no intrinsic elevation
5	10/ 1/57	50	F	Paroxysmal tachycardia	Not palpable	30% concentration 4 discrete foci 2.5 times normal	10/ 1/57	4.0	12/ 2/57	90	32% concentration no intrinsic elevation
6	3/27/57	51	F	Sinus tachycardia	Small, palpable and nodular	43% concentration nodular areas, 3 times normal function	3/27/57 4/ 3/57	5.0 5.1	9/ 4/57 2/28/58 7/15/58	100	17.5% concentration no intrinsic elevation
7	4/22/57	64	F	Tachycardia heart failure	Palpable and nodular	50% concentration nodular area, 5 times normal function	4/23/57 4/27/57	4.2 4.0	9/ 9/57 12/31/57	90	10% concentration no intrinsic elevation
8	5/14/57	54	F	Sinus tachycardia	Not palpable	29% concentration 3 cm area twice normal function	5/15/57 5/21/57 5/28/57	2.3 4.0 4.0	11/ 4/57	100	36.4% concentration no intrinsic elevation
9	5/27/57	72	F	Sinus tachycardia heart failure	Moderately enlarged and nodular	71% concentration nodular areas, 4 times normal function	5/28/57 6/ 4/57 9/30/57	4.0 4.0 5.0	9/26/57 6/10/58	100	23% concentration no intrinsic elevation
10	6/20/57	68	F	Heart failure	Not palpable	63% concentration 3 times normal function	6/21/57 6/26/57 7/ 2/57	5.0 4.15 5.2	6/25/58	75	21% concentration no intrinsic elevation
11	6/27/57	48	F	Heart failure	Not palpable	41% concentration 3 foci 3 times normal function	6/27/57 7/ 3/57	4.0 4.16	9/25/57	75	22% concentration no intrinsic elevation
12	6/30/57	72	F	Heart failure	Not palpable	47.5% concentration 4 cm area 3 times normal function	7/ 5/57 7/10/57	4.04 4.0	11/12/57	90	10% concentration slight intrinsic elevation
13	7/30/57	60	F	Sinus tachycardia heart failure	Not palpable	30% concentration 3 cm area, 2.5 times normal function	8/ 2/57 8/ 6/57 1/ 9/58	4.0 4.0 4.0	1/10/58 6/ 1/58	90	20% concentration no intrinsic elevation
14	7/30/57	55	M	Angina pectoris	Not palpable	28% concentration 3 cm area, 3 times normal function	7/30/57 8/16/57	4.0 4.0	9/ 4/57 11/ 5/57	100	25% concentration no intrinsic elevation
15	11/25/57	64	M	Heart failure	Not palpable	30% concentration 4 cm area 3 times normal function	12/ 3/57 12/ 7/57	6.0 6.0	1/25/57 2/22/57 6/10/58	90	32% concentration no intrinsic elevation
16	12/ 4/57	34	F	Tachycardia	Small, palpable and nodular	33% concentration 3.1 cm areas, 3 times normal function	12/10/57 12/19/57	4.0 4.0	2/14/57	100	28% concentration no intrinsic elevation
17	2/ 7/58	57	M	Angina pectoris	Not palpable	50% concentration, 3 foci 3 times normal function	2/ 5/58 2/11/58 2/18/58	5.0 5.0 5.0	3/ 4/58	90	48.2% concentration no intrinsic elevation
18	2/26/58	52	M	Angina pectoris	Not palpable	40% concentration 2 cm focus 2 times normal function	2/26/58 3/ 6/58 3/15/58	5.0 5.0 5.0	4/24/58	100	32% concentration no intrinsic elevation
19	12/10/57	50	F	Sinus tachycardia	Small palpable and nodular	24.8% concentration 3 cm focus, 3 times normal function	12/10/57 12/17/57 12/24/57	4.0 4.0 4.0	1/28/58 3/ 8/58	100	20.8% concentration no intrinsic elevation
20	5/ 7/57	55	F	Heart failure	Not palpable	45% concentration 2 cm focus 4 times normal function	5/13/57 5/18/57 5/24/57 5/31/57 10/ 1/57 10/17/57	2.3 5.0 2.1 5.25 4.0 4.0	6/12/57 9/30/57	None patient died 11/1/57	40% concentration 2 cm focus 4 time normal function
21	10/14/57	48	M	Heart failure angina pectoris	Not palpable	36% concentration 3 foci 3 times normal function	10/15/57 10/21/57	4.0 4.0	11/ 1/57	None	Patient died 11/15/57
22	6/20/57	72	F	Heart failure auricular fibrillation	Not palpable	31% concentration 2 cm area twice normal function	6/21/57 6/26/57 7/ 2/57	4.12 4.0 4.0	6/ 1/58	75	32% concentration no intrinsic elevation
23	6/23/58	32	F	Heart failure auricular fibrillation	Not palpable	41.5% concentration multiple foci 2.5 times normal	6/26/58 7/ 1/58	5.2 7.1	8/28/58 10/ 5/58	90	35% concentration no intrinsic elevation
24	4/29/58	65	F	Sinus tachycardia	Nodular	46% concentration 1 focus 3 times normal function	5/13/58 5/19/58	5.0 4.0	6/27/58 9/ 4/58 1/ 6/59	100	27% concentration no intrinsic elevation
25	12/ 9/57	54	F	Sinus tachycardia, heart failure	Nodular	38% concentration 1 focus 4 times normal function	1/10/58 1/17/58	4.0 4.0	1/21/58 2/25/58 5/ 8/58	75	11.5% concentration no intrinsic elevation

cessfully for precise location of the small toxic adenomas sometimes present in young children[9] In some patients the toxic adenoma was large enough to be demonstrated with the scintillation counter This is illustrated by the findings in the patient in case 18 at the time of the first tracer study (fig 1) and after isotope therapy (fig 2) This patient's percentage concentration in 24 hours (uptake) was 40% at the time of the first tracer study and 41 5% after elimination of the adenoma and recovery of the entire gland from the initial blocking effect of the radiation

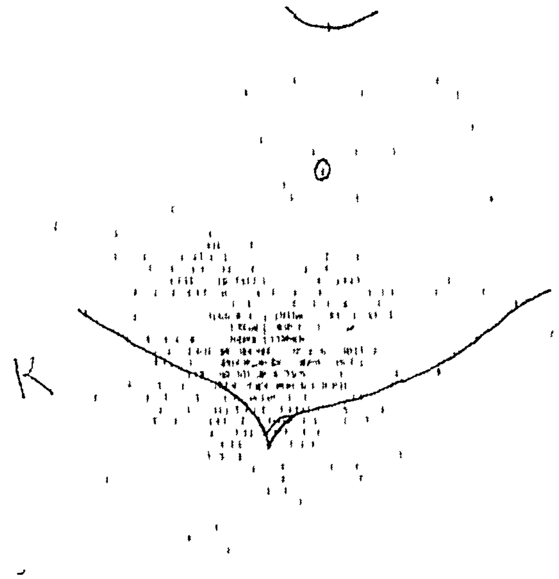

Fig 1 (case 18)—Scintillation scan pattern before treatment with I^{131}

The therapeutic procedure followed in this case is typical of that in all the cases The basic concept is an attempt to destroy the adenomatous area or areas with as little damage as possible to any residual normal tissue To this end a small initial dose is administered In this case there was a rather large gland with a large adenoma, about 2 cm in diameter, having about twice normal intrinsic function With these considerations the patient received an initial increment of 5 mc of I^{131} on March 1, 1958 A retention measurement made at the end of five days showed 39 4% The patient was given a second increment of 5 mc at this time After an interval of one week, on March 13, 1958, the patient's retention of the total dosage was 47 2%, indicating that he had accumulated 33 5% of the second increment With this much iodine avidity still present in the gland, it was thought best to give a third increment, which was done The final measurement of the therapy series was performed on March 27, 1958, two weeks after administration of the third 5 mc This showed a total retention of 26%, or a 4% accumulation of the third increment of the series The final study of this series was conducted April 24, 1958 The patient was found to have a retention of about 25 μc remaining from his isotope therapy The gland was completely outlined with the small-aperture counter

The distribution of the activity was found to be relatively uniform, with a slight excess in the right anterior aspect The size, shape, and position of the gland were not significantly changed The patient's blood pressure was 130/80 mm Hg His pulse rate at this time was 84 per minute, and he reported that he was in good condition and had suffered no anginal pain for the previous two weeks No further isotope studies were conducted until he was brought in again for the study of June 19, 1959, to evaluate his present condition

Comment—This illustrates the type of procedure which we have found the most satisfactory in dealing with anginal and other types of cardiotoxic disease The adenomas are first located and their intrinsic function measured and recorded A series of small doses is given under the control of clinical observation and retention measurements Sometimes an adenoma not previously noticed will either become active or be uncovered as the known foci are eliminated In these cases one or two small additional increments may be needed Growth of the adenomas tends to destroy normal thyroid tissue,[10] so that, in some cases, after the adenomas are eliminated, even without significant destruction of the residual normal tissue by radiation, the residual may not be adequate for the patient's

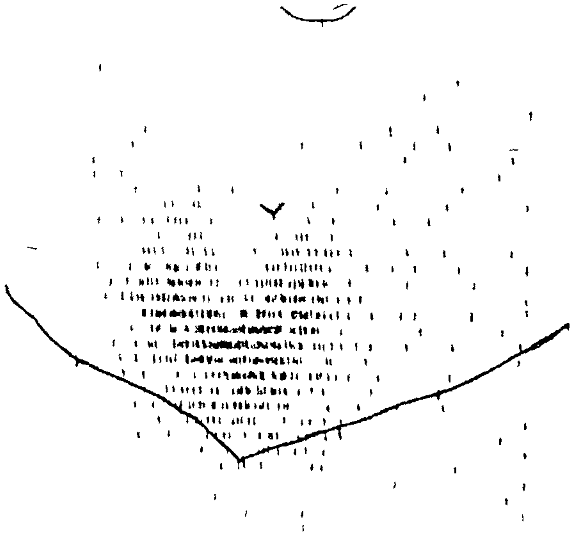

Fig 2 (case 18)—Scintillation scan pattern after treatment with I^{131}

needs In these cases elimination of the adenoma, if it is relatively small compared to the balance of the gland, may, as in the case illustrated, permit the remaining thyroid to regain function to a point where the patient's total thyroid function is slightly higher than that found in the original measurement before elimination of the toxicity As measured by tracer techniques at the end of therapy, only one person presented a total thyroid function below the normal range

The improvement or lack of improvement was studied by both subjective and objective methods There was marked improvement in all cases except two, in which the patients died of myocardial infarction Autopsy demonstrated a ruptured heart in one case, 21, at the site of recent infarction A radioautograph revealed elevation of intrinsic function in this case

Summary and Conclusions

Forty-three patients with heart disease that responded poorly to conventional therapy were studied by radioiodine (I^{131}) tracer technique, and 25, or 58%, were found to have elevated intrinsic thyroid function A diagnosis of hyperthyroidism complicating heart disease was not made in any case prior to tracer studies These 25 patients were given I^{131} therapy conservatively and cautiously as outlined, the idea being for the patient to end treatment with normal thyroid function rather than a state of hypothyroidism This was accomplished and was accompanied by a rewarding and satisfactory improvement in the 23 surviving patients Nine patients did not require any therapy after I^{131} treatment In several of the cases the total I^{131} concentration improved in the gland after elimination of the toxic area

When cardiotoxic thyroid disease occurs, either alone or in the presence of other forms of heart disease, it may be difficult to detect From our small series of cases it would appear that cardiotoxic thyroid disease may be present in a sizable percentage of patients with heart disease that responds poorly to medical treatment I^{131} tracer technique will detect concealed thyroid disease When cardiotoxic thyroid disease is found to be present, our series of cases would indicate, excellent results may be obtained by creating a normally functioning thyroid gland with cautious and conservative I^{131} therapy for the elimination of the toxic foci

280 W Maple (Dr Hammonds)

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PROGRESS IN ROENTGENOLOGY AND ROENTGENO-THERAPY—As to the danger of this method of investigation, I cannot understand how it has come to be exaggerated to such a degree I have seen and made thousands of screen examinations, and I have never seen the slightest accident to a patient The chronic dermatitis of the operator is now rarely seen unless dating from injury received in the early days of Roentgenography, when sufficient protection was not used, and before the temerity of ignorance had given place to prudence—J Belot, Recent Progress in Roentgenology and Roentgeno-Therapy, *Archives of the Roentgen Ray*, Paris, vol 12, May, 1908, page 344

Prophylactic and Other Treatment for "Histaminic," "Cluster," or "Limited" Variant of Migraine

Comparative Study, Therapeutic Recommendations, and Discussion of the Nature of the Syndrome

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A comparison was made between the main therapeutic measures advocated for this well defined clinical syndrome The methods compared in 52 patients were sphenopalatine ganglion anesthesia, histamine desensitization, and prophylactic ergotamine tartrate The efficacy of the first two methods was shown to be equally doubtful, in particular because each attack and each cycle of headaches are self limiting Ergotamine tartrate, while ineffective during the attack, provided excellent prophylaxis for the duration of the cycle The required dosage exceeded the conventional margin of safety for this drug yet did not produce any toxic effects The results with massive oral prevention were equal to those obtained parenterally "Limited migraine variant" or "hemicrania limitata" seem the most descriptive, comprehensive, and internationally acceptable terms for this many named condition

For some 50 years accounts have appeared of a typical and by no means uncommon clinical entity which is often mistaken for tic douloureux or dubbed 'atypical facial neuralgia' but which displays a mechanism more closely allied to migraine The syndrome has given rise to a confusing number of names, including, among many, "sphenopalatine neuralgia and 'lower half headache' (Sluder, 1908),[1] 'erythroprosopalgia" (Bing, 1913),[2] erythromelalgia of the head" and 'histaminic cephalgia' (Horton, 1939 and 1941),[3] and "cluster headache' (Kunkle, 1952)[4] The latter term heads a contemporary review by Friedman and Mikropoulos,[5] while Bickerstaff,[6] even more recently, has revived the name "periodic migrainous neuralgia" (Wilfred Harris, 1926)

The purpose of the following study of 52 patients with this syndrome was to evaluate the various medical means of therapy advocated up to the time of this writing Surgical intervention has proved disappointing As a result, it appears that older methods may be discarded in favor of vasoconstrictor agents[7]

But to be of value treatment has to be prophylactic, a point made only by Symonds[7d] and Bickerstaff[6] Prophylactic doses of ergotamine tartrate may be given orally[7c] and must be sufficiently large,[8] even excessive by some standards, although they have been found safe in my experience

Clinical Description and Differential Diagnosis

The criteria for inclusion in this study may also serve as clinical description and differential diagnosis

Site of Pain —The pain must be strictly unilateral, originating in or around one orbit, possibly at the root of the nose, and must spread to temple, mastoid, occiput, and maxilla, or occasionally to the palate and the neck, without trigger action such as occurs in trigeminal neuralgia

Time Relations—A single attack must not exceed three hours, as do attacks of migraine or tension headache, but must last longer than a few seconds, unlike attacks of trigeminal neuralgia No limit was set on the frequency of such attacks during a 24-hour period The attacks were noted to occur in clusters"[4] or 'bouts"[7d] lasting weeks

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From the Division of Neurology Department of Internal Medicine Kaiser Foundation Hospital to months, separated by intervals lasting weeks to years during which the patient was free of attack

Autonomic Concomitants—At least one of the following features must occur during an attack conjunctival hyperemia, lacrimation, rhinorrhea, or stuffiness of the nose, confined to the side on which the pain occurs Horner's syndrome[2] or ulceration of the cornea[8] was not encountered Visual failure such as occurs in glaucoma, nausea, and vomiting must not be present

Neurological examination was performed in all subjects Most of the patients had been referred to the neurologist after a medical or rhinological examination or both or were so examined subsequently

Analysis of Fifty-Two Cases

Of the 52 patients included in the study, 45 were men and 7 were women In only one instance were relatives included in the study (a mother and her son) All patients were between 10 ond 65 years of age at the time of onset of the attacks, the maximum number of cases began in patients between the third and fifth decade of life

At the time they were seen, the patients had had between 0 and 20 previous attacks, the majority having had 2 to 3 previous attacks Previous cycles had lasted from 2 to 24 weeks The cycles occurring at the time of this study lasted from one week to over one year, the majority lasting one to two months Intervals between cycles were from two months to 47 years, usually one to two years Most patients had one or two attacks a day, although some had more and two patients had so many that they could not be counted The number of patients in whom the right side was involved equaled the number in whom the left side was involved

Of the patients, 75% smoked 20 or more cigarettes daily Associated or preceding otorhinolaryngeal conditions, e g , sinusitis, septum deviation, or frequent nasal colds, occurred in 75% of patients Eight patients could reasonably be said to suffer from anxiety or compulsion Two of these were receiving treatment intermittently for peptic ulcer One additional patient, on the borderline of being compulsive, had a myocardial infarction during the period of observation

Histamine Sensitivity—Twenty-six unselected patients were, or had elsewhere been, subjected to the provocative histamine test,[3] the injection of 0 3 or 0 6 ml of histamine diphosphate solution, 0 275 mg per milliliter The patients were told nothing of the nature or possible effect of the test injection A reaction was considered positive when within one-half hour the patient experienced pain similar to that for which he had sought help Many patients were asked to lie down during the one-half hour in which the test took place, a posture which is in itself conducive to recurrence of the pain Only 5 of the 26 patients showed positive or at least doubtfully positive reactions Two of the five had been subjected to the same test elsewhere (one by an associate of Dr Horton at the Mayo Clinic) Of the remaining three, only one experienced a full-blown attack, the other two complained only of minor discomfort in the usually affected site

Therapeutic Methods and Results

The medical therapeutic measures discussed by various authors are best classified under three headings (1) cocaine blocking of the sphenopalatine ganglion,[1] (2) histamine desensitization,[3] and (3) vasoconstricting agents of either the parenteral type[7a] or the oral type[10] The study of these 52 patients began before an adequate prophylactic treatment was introduced by Symonds[7a] Hence it was the last 18 patients who were so treated, 15 of them exclusively so In 16 patients failure of one type of treatment led to trial with another Seven patients received no treatment because they presented themselves after termination of their cycle

Cocaine Blocking of the Sphenopalatine Ganglion[1]—This form of treatment, used in 25 patients, consisted of leaving a nasal cotton applicator which had been soaked in a 5% hexylcaine hydrochloride solution at the posterior nasopharyngeal wall for 10 to 15 minutes per session once or twice weekly Treatment was discontinued after complete or no relief was afforded within 2 to 30 sessions A second course of treatment was given to two patients Absolute alcohol was injected into the region of the sphenopalatine ganglion after procaine infiltration in two patients, in one of these, a neurosurgeon finally divided the greater superficial petrosal nerve

Histamine Desensitization[3]—This treatment, used in 14 patients, consisted of subcutaneous injection of histamine diphosphate (0 275 mg per milliliter) in fractions increased daily from 0 05 to 0 35 ml Such injections were administered over varying periods of time and were never given in amounts greater than 1 ml Ten of the patients had had similar courses previously A positive response to the histamine test was not requisite to the selection of this form of treatment

Prophylactic Parenteral Injections of Ergotamine Tartrate[7d]—The contents of one ampule (0 25 mg or 0 50 mg) of ergotamine tartrate was given subcutaneously in 10 patients by the patient or another lay person, at bedtime only if the attacks were nocturnal Diurnal attacks were treated preventively by a like injection after the patient arose in the morning After about one week the patient was encouraged to discontinue the injections but to resume them immediately for another few days if pain recurred

Prophylactic, Orally Given Ergotamine Tartrate[10].—In eight patients, 3 to 4 and occasionally more ergotamine tartrate (Cafergot) tablets were given at bedtime for nocturnal attacks, and this dose was repeated when the patient arose in the morning if he had diurnal attacks. The treatment was first used tentatively and, if no relapse interfered, was discontinued, as with the group given parenteral injections.

For patients receiving these four types of therapy, results were considered "good" when the patient remained free from attacks for longer than one month, beginning during a course of treatment or immediately after its conclusion. A few patients reported slight local discomfort, as though an attack were beginning. By "fair" was meant a considerable reduction in frequency and severity of attacks. Results were termed "poor" if no change was appreciable.

The results were as follows: Of the 25 patients in whom cocaine blocking of the sphenopalatine ganglion was performed, 12, or 54%, showed good results, 5 showed fair results, and 5 showed poor results; there was no information about 3 of these patients. Of the 14 in whom the method of histamine desensitization was used, 6, or 43%, showed good results, 3 showed fair results, and 5 showed poor results. The 10 patients given subcutaneous injections of ergotamine tartrate prophylactically all showed good results.

Report of Cases

Case 1.—A 50-year-old man, a rating examiner in the United States Navy, had one or two attacks of severe pain lasting two to three hours in the right temple, mandible, and orbit, spreading to the neck. These attacks occurred each year for about 15 years, usually in the winter, and nearly daily for about four weeks. Ipsilateral congestion of nostril and conjunctiva and lacrimation were present during the attack. He had three or four nasal colds every year but had no other history pertaining to the ear, nose, or throat. He smoked 40 cigarettes a day. He had seen about five physicians whose various treatments had no results. The onset of the present cycle occurred ten days before he was seen. Examination showed nothing remarkable. The patient was given 0.25 mg. of erogtamine tartrate (Gynergen) orally at bedtime and had no attacks for three days. Then attacks occurred 13 and 18 hours after injection, respectively, on two subsequent consecutive days. He was advised to take a second dose of ergotamine tartrate in the morning, which he did only once. He suffered no further attacks. Prophylactic injections were discontinued after two weeks, and no recurrence took place.

Case 2.—For three weeks, a 47-year-old janitor had daily, mostly nocturnal, attacks of severe pain in the right orbit, forehead, temple, and even the neck, congestion of right eye and nostril, lacrimation, and rhinorrhea lasting one-half to two hours. The patient paced the floor during attacks. He had had a similar cycle 17 years earlier which lasted six to eight weeks. He had never had any nasal trouble. He smoked 40 cigarettes a day. Examination showed no remarkable findings. The patient was treated with 4 ergotamine tartrate (Cafergot P.B.) tablets at bedtime. He was seen the following day, six days after his first visit, and one year later. Medication was continued for less than two weeks. At the time of this writing, he had had no attacks since the first visit.

Comment

The self-limiting nature of this migraine variant tends to vitiate the evaluation of treatment aimed at long-term results. An attack may be shorter than the time for a remedy to become effective and the natural cycle shorter than a course of treatment. The patients usually seek help after the cycle has been running for one or two weeks, and two to four additional weeks are required for a course of either cocaine blocking of the sphenopalatine ganglion or histamine desensitization; thus, claims for the effectiveness of either approach justify skepticism. Patients in this study were, if anything, slightly better off with blocking of the sphenopalatine ganglion than with histamine desensitization. One patient needed only one or two cocaine blockings to terminate his respective cycles.

The "histaminic cephalgia" hypothesis of Horton[3] is based on the assumptions that histamine concentration in the affected area is excessive, a positive response to the histamine test proves histamine to be the pathogenic agent, and "successful" histamine desensitization proves the histaminic nature of the attacks. None of these assumptions was justified at the time of this writing. Chronic inflammation may cause a local accumulation of mast cells, the body's main repositories of histamine, and it may be significant that 75% of the patients in this study had past or present nasal disorders, while in two others tooth extraction coincided with termination of a cycle. Abnormal sensitivity of the local blood vessels to histamine might explain positive results of the provocative systemic histamine test. Of five patients with positive response to histamine, two had good results from subsequent histamine treatment; in another with doubtfully positive response, the result of such treatment was fair.

There is some confusion in the literature regarding the size of the dose of histamine diphosphate; the amount used in this study, 0.1 to 0.2 mg. given subcutaneously, may have been too small, but the 0.35 mg. most recently advocated by Horton[3c] tends to produce headache in patients suffering from migraine. Wolff and many others[11] have questioned the specificity of the test and that of the treatment ("as specific as insulin")[3b] as well.

Throughout the years Sluder's views have come under even greater criticism than Horton's. Like histamine desensitization, cocaine blocking of the sphenopalatine ganglion has been used indiscriminately and has fallen into disrepute. But it is not impossible that vasomotor fibers passing from the brain stem to the sphenopalatine ganglion exert some control over the vascular area involved in this syndrome.[12] Repeated "blocks" with cocaine, although superficial and haphazard, may lessen excitability in this efferent parasympathetic system. An effect on afferent fibers in the same nerves seems less likely.

Most observers agree that this variant, like migraine proper, is vasodilator in nature, but the features that distinguish the two conditions and make them even incompatible with one another are the characteristic time pattern, the autonomic concomitants, and the absence of nausea and vomiting. Further, there is the preference for erect position and the restless pacing of the patient during the attacks described by Sluder and Horton, which are not observed in migraine proper (Wolff).[12c] True migraine was not found to be a complicating or hereditary feature in any of the patients studied here, nor were suicidal tendencies[3] encountered. In my experience, ergot given by any route had no effect during acute attacks, or the effect was not clearly distinguishable from the spontaneous cessation of the attack.

The logical, and so far the only practicable and effective, approach seems to be prevention of the acute attacks. Short-term prophylaxis by the parenteral administration of ergotamine tartrate, as first suggested by a patient of Symonds[7d] and confirmed by Bickerstaff,[8] is one of the answers to the pain. But I have reason to believe that use of the parenteral route will safely yield to prophylactic oral medication with ergotamine, first suggested by Ekbom.[7c] The doses required, however, are larger than those conventionally thought permissible, i. e., usually 3 to 5 tablets, each containing 1 mg. of the drug, once or twice daily, sometimes for several weeks. One patient required up to 8 tablets twice daily for full control. As Symonds[7d] has shown, the dangers of permanent vasoconstriction have been greatly overrated. Should premonitory signs appear, administration of the drug would be discontinued, but no untoward side-effects were observed in this series. The mechanism of prophylaxis is not clear. Protection lasts at least 12 hours.

Methods of treatment other than drug therapy or surgical intervention should be mentioned. Campbell's[13] results with immobilizing the cervical spine were probably coincident with spontaneous cessation of the cycle. The syndrome here discussed is to be distinguished from the cervical syndrome, where the occasional pain in the upper portion of the face is constant rather than semiparoxysmal.

The value of psychiatric treatment is not established. Emotional tension is not likely to be an important factor in the single, mostly nocturnal, attacks, but periods of anxiety in persons of suitable temperament[14] may possibly coincide with the cycle. Major abnormalities in personal make-up were infrequent among the patients studied, nor was any of them able to associate the cycle with particularly difficult life situations. As has been noted, migraine proper was not a complicating feature in any of the cases reported here. Engel,[15] who identifies "primary atypical facial neuralgia" with hysterical conversion mechanisms, presents no case with the characteristics of this variety of syndrome. Finally, the smoking habit is too common to serve as a causative factor or as an argument in favor of psychogenesis.

The question of terminology should be settled. As the condition probably neither is caused by histamine nor has the distribution of neuralgia but shows definite affinities to migraine, with characteristic limitations in area and duration, the term "limited migraine variant" or "hemicrania limitata" is suggested; "cluster headache," while more snappy, describes only its periodic incidence.

Summary

Various authors have under various names described attacks of severe unilateral head and face pains which, by their limitations in area and duration and by their characteristic autonomic concomitants, form a typical clinical pattern easily distinguished from migraine, trigeminal neuralgia, and other painful conditions of this region.

The symptoms of 52 patients suffering from such attacks were analyzed, and treatment was given by one or more of the following methods: (1) histamine desensitization, (2) cocaine blocking of the sphenopalatine ganglion, or (3) prophylactic ergotamine tartrate, given either orally or subcutaneously.

Favorable results that occurred with the first two methods may well have coincided with the spontaneous cessation of a cycle of attacks as characteristic of this affliction. The old cocaine treatment of the posterior nasopharyngeal wall seemed at least as effective as histamine desensitization.

The satisfactory measures were prophylactic injection or large oral dose (3 to 5 tablets twice a day) of ergotamine tartrate. In the 18 patients so treated, attacks were prevented for a minimum of 12 hours; no side-effects were seen. "Limited migraine variant" or "hemicrania limitata" may be the most adequate term for this condition.

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Treatment of Acne Vulgaris

Use of Systemic Antibiotics and Sulfonamides

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The authors have studied the effectiveness of selected orally administered antibiotics and sulfonamides in treating certain moderately severe to very severe forms of acne All patients had failed to respond satisfactorily to other measures However, the systemic antibacterial agents were used as supplementary, rather than substitute, methods of therapy Evaluation is made of the nature and degree of side effects of long-term and short-term use of these drugs There were 312 courses of oral therapy administered from 2 days to 6 years 9 months to 208 patients The results were excellent in 13 of the courses good in 196, fair in 86 and poor in 17 Side effects included Candida albicans vaginitis (the only severe complication requiring therapy) diarrhea, mild nausea, and changes of total or differential white blood cell count Only 27 patients had complaints which necessitated the discontinuation of the drug used

No well informed physician, parent, or patient today will challenge the statement that acne vulgaris is often a horrible disease, which can ruin the life, scar the skin, and warp the psyche of many among the millions of adolescents it affects It is also indisputable that the available local measures, excellent as they are in many cases, are often inadequate and that roentgenologic treatment is a great therapeutic weapon in such cases

It is our conviction, based on ample evidence, that properly administered, properly shielded roentgenologic treatment presents little or no danger to either the person or the race treated, when it is confined to the dosage range and to the quality regularly used by competent dermatologists in the treatment of acne Nevertheless, there is such a hysterical attitude toward roentgenologic treatment on the part of many segments of the public and some physicians that dermatologists, whenever possible, generally refrain from using it and search for other measures to relieve the suffering and disfigurement of their patients

Our own experiences and those of other dermatologists have shown that the systemic administra-

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tion of the broad-spectrum antibiotics and of the "safer" sulfonamides has done more to improve the management of acne vulgaris than any other measure during the past 10 years.[1] Here too, however, the long-term administration of selected effective antibiotics or sulfonamides is necessary to maintain the morbidistasis (suppression of disease manifestation without necessarily curing the underlying disease) of acne vulgaris which usually heals of itself sometime between the ages of 13 and 23 years. Unfortunately, here also, the public and some physicians have developed certain unjustifiable as well as some justifiable fears. The effective long-term treatment of acne vulgaris may be delayed or prevented by this unjustified resistance to the administration of systemic antibiotics and sulfonamides or both.

In view of this, we thought it would prove useful to substitute some facts and experience for fancies and fears in this field of acne management. The present paper reports the results of a study of the effectiveness of selected orally administered antibiotics and sulfonamides in the management of acne vulgaris, and reports and evaluates the nature and degree of the side-effects encountered in the long-term and short-term use of such drugs. The indications and rationale of systemic antibiotic or sulfonamide therapy, the particular drugs and dosage schedules used, and the practical therapeutic applications are discussed.

Indications and Rationale

In the more severe forms of acne, primarily the pustular and inflamed cystic varieties, secondary bacterial infection is believed to play a contributing role.[2] Coagulase-positive staphylococci (micrococci) can frequently be recovered from acne lesions, and these, possibly together with other entrapped aerobic and anaerobic micro-organisms, may or may not be etiological factors in the clinical lesion. On the basis of this concept of various modes of possible pathogenesis, the beneficial effects of orally given antibiotics in acne may be the result of their action on the particular micro-organism in situ, however, the antibacterial drugs in some cases may be effective through their action on such various remote foci of infection as the teeth, sinuses, and tonsillar crypts. In addition to the antibacterial mode of action there may be an entirely different pharmacological effect resulting from an antibiotic. It is known, for example, that certain antibiotics contain a growth factor which is used advantageously in animal husbandry. In addition to their antibacterial properties, these drugs may have other actions which may exert a beneficial effect in the treatment of acne. We do not substitute systemic antibacterial agents for the standard methods of therapy, however, but use them as supplementary treatment.

Patients and Dosage

The 208 patients included in this study presented no known contraindications to the administration of the particular drugs, although they had moderately severe to very severe pustular and cystic acne, or both, or acne conglobata. (This otherwise unselected number of patients represents only a fraction of our patients with acne, treated with systemic antibacterial agents during the last 10 years.) All were patients who had failed to respond to other measures and were therefore started on therapy with antibacterial agents. Patients with acne vulgaris that could easily be managed with standard therapy were not included. No attempt was made to identify or culture the bacteria in any of the lesions or to ascertain their sensitivity to the various antibiotics and sulfonamides that were contemplated for use. Although this would have been theoretically desirable, it was not feasible or necessary, as our results showed. All patients received various types of conventional treatment for acne in addition to the orally given antibacterial agents.

Varying dosage schedules were evaluated to determine the optimum initial dose for a satisfactory suppression of the acne lesions and prevention of the occurrence of new ones. The following schedule has generally proved effective with the orally given broad-spectrum antibiotics and easiest for patient and physician to remember: 250 mg. 4 times daily for four days, 3 times daily for three days, and 2 times daily for seven days. After this 14-day period, the therapeutic response was evaluated and the daily dose decreased or increased as considered necessary to maintain adequate control.

Sulfisoxazole therapy is started at 4 Gm. daily, after which the dose is gradually reduced according to the principle just outlined for antibiotics. Our experience with sulfadimethoxine is still somewhat limited, we began with 0.5 Gm. twice daily for one week and then reduced the dose to 0.5 Gm. daily.

Individual response to treatment varies greatly and, therefore, there is no prescribed routine schedule which is regularly applicable after the initial period of therapy as outlined previously. The goal in treatment is to ascertain the least amount of drug that can be used and still maintain a desirable morbidostatic effect. Usually there is a definite effective dosage level for each antibiotic or sulfonamide for each patient, which can be ascertained during the first weeks that a patient is treated. Most patients have a minimal effective therapeutic dose (morbidostatic dose) below which an exacerbation of acne will occur while standard topical and other treatment (desquamating agents, diet, acne surgery, and hormone therapy) is continued. We have found that the response obtained with the use of conventional acne therapy alone differs from that with the use of such therapy plus orally given antibiotics or sulfonamides in cystic and pustular forms of the disease Dosage may have to be increased temporarily because of flare-ups due to dietary indiscretion, premenstrual, and other causes, often unknown One patient may have excellent control with 125 mg of a wide-spectrum antibiotic daily, another with 125 mg every other day, another may require 500 mg daily, and another may be given smaller doses of an antibiotic over a period of weeks or months and eventually be treated with only topical agents until the end of his acne age At times it is necessary to change from one antibacterial agent to another or to use the two concomitantly At each visit every effort should be made to lower the dosage, yet maintain the beneficial effects This often may be a slow process requiring months and sometimes years

It is advisable to do a complete blood cell count periodically while patients are taking any of the antibacterial agents and a complete blood cell count and urinalysis while they are receiving a sulfonamide drug In the beginning, when the larger dosages of these drugs are being administered, these studies should be done every two weeks, when the dosage is lowered, repetition of the tests every three to six weeks usually suffices Orally given vitamin B complex with cyanocobalamin plus orally given nystatin are administered in an effort to prevent the reported side-effects[3] of vitamin B deficiency and the overgrowth of yeast organisms

The mechanism by which active candidiasis (moniliasis) develops in a patient after antibiotic therapy is still a matter of speculation Various theories to explain the activation of a quiescent focus in the so-called Candida organism carrier include (1) modified ecology in which antibiotic-resistant micro-organisms flourish when the antibiotic-sensitive organisms are lost from the normal flora, (2) direct Candida growth-stimulating effect of the antibiotic, (3) local allergy and skin or mucous membrane damage followed by local loss of specific tissue resistance to the Candida organism, (4) impairment of vitamin production leading to a loss of resistance, (5) flare-ups of old sites of Candida infection analogous to biotropism, and (6) combinations of these factors

Seventy-five of our patients received the orally administered medicaments for over six months The longest period was six years and nine weeks (table 1)

Evaluation

The following details of our observations are submitted to substantiate our general conclusions about the high effectiveness and low risks of prolonged systemic antibiotic therapy in acne vulgaris Development of clinical resistance to treatment with use of a certain antibiotic was not a problem except in some of the occasional patients who had a prolonged lapse in treatment This group included those who did not return during the summer months because the acne was ameliorated as a result of regular sun exposure, and they continued with only the minimal topical therapy they found necessary Another such group included those who obtained a good response with the combined drug and topical treatment, stopped taking the antibiotic, and undertook self-treatment without supervision for several months with only the topical agents that had been prescribed previously When the patients returned after a prolonged absence, we found that frequently they did not respond as well to the same antibiotic at the previously effective dosage, whereas the substitution of another antibiotic was often successful It was often necessary to begin again with the larger dosages used initially

Evaluation and recording of effectiveness of response were based on the clinical appearance of the patient and to a lesser degree on the patient's opinion The response was classified as excellent when there was an estimated 91 to 100% improvement (this included prevention of the formation of pustular and cystic lesions plus the suppression of papular lesions), as good when there was an estimated 76 to 90% improvement, as fair when there was an estimated 26 to 75% improvement, and poor when the improvement was estimated at 25% or less

TABLE 1 —*Length of Time 208 Patients Received Orally Administered Antibiotics and Sulfonamides, or Both*

Duration of Therapy Mo	No of Patients
1 or less	50
2 3	52
4 6	28
7 9	23
10 12	7
13 17	11
18 22	18
23 27	6
28 32	2
33 39	3
40-46	3
47 53	1
54-60	3
61-67	0
68 74	0
75-81	1
Total	208

Among the drugs used, the broad-spectrum antibiotics, particularly of the tetracycline group, were the most frequently prescribed (table 2) It is difficult to determine which of the antibiotics used was the most reliable in providing satisfactory acne control, and which could be depended on most to produce the least undesirable effects Twenty-seven patients had complaints leading to the discontinuation of a particular drug and the substitution of another drug after an appropriate rest period (usually two to three days) Six of these patients also had complaints with two or more of the medicaments when tried successively

The length of time a drug was used before undesirable effects were noted varied from one day with urticaria to 54 weeks with Candida albicans vaginitis In all but one instance (Candida albicans vaginitis) the undesirable effect occurred within 9 weeks after starting medication, and 43% occurred within 10 days The incidence of complaints was highest with chlortetracycline and oxytetracycline therapy,[4] although the total number of these cases does not permit significant statistical analysis

Nine other patients complained of frequent and loose stools and mild nausea, or both, within one week after starting the medication, but all nine were able to continue treatment at the same or lower dosage levels This raised the unresolved question of whether in any or all of these patients the nausea and loose stools were secondary to treatment or coincidental as the result of some intercurrent illness (At the time of the year that some of these reactions occurred, the incidence of similar gastrointestinal complaints in patients who were not on antibiotic therapy was high)

If the signs and symptoms (frequent bowel movements, loose bowel movements, nausea, abdominal cramping, and indigestion) are mild, one of several approaches may be attempted (1) the antibiotic may be discontinued temporarily and later reinstated at a lower dose, (2) the patient may be instructed to take the medication with food or cold milk (after which the signs and symptoms often disappear), (3) the drug may be continued at a lower dose, or (4) another antibiotic may be substituted

If side-effects force the discontinuation of a particular drug, recovery without specific treatment usually occurs Another antibiotic may be substituted in most cases Only six of our patients had difficulties with two or more of the drugs None developed a major systemic illness during the period of therapy with antibiotics or sulfonamides Our impression is that the drugs did not prevent intercurrent viral infections such as the common cold and influenza We were not able to determine if the patients on long-term therapy had a lower or higher incidence of such other bacterial infections as streptococcic throat infections and otitis media There were no overwhelming or debilitating bacterial, fungal, or viral infections from the emergence of resistant or nonsusceptible organisms [5]

Seventeen patients had changes in the total white blood cell or differential counts [6] consisting of such deviations as a total white blood cell count of above 10,000 or below 5,000 per cubic millimeter, a lymphocyte count of above 45%, or an eosinophil count of above 5% These changes were transient and did not depend on drug dosage The medication was continued in all cases The effects of long-term administration of the broad-spectrum antibiotics on the peripheral blood count is the subject of another report [7]

TABLE 2 —*Effectiveness of Drugs Used in 208 Acne Patients*

			Response*				Undesirable Effects†																	
Drug	Duration of Therapy	No of Times Drug Was Prescribed	Excellent	Good	Fair	Poor	Abdominal Cramps	Backache	Diarrhea	Chills	Emesis	Fever	Indigestion	Nausea	Papular Eruption	Genitocrural Pruritus	Vaginal Pruritus	Stomatitis	Urticaria	Vertigo	Weakness	Candida albicans Vaginitis	No of Times Side-effects Occurred	% of Patients with Side-effects
Carbomycin	5 wk	1		1																			0	0
Chloramphenicol	8 32 wk	8		7	1																		0	0
Chlortetracycline	2 days to 19 wk	7	1	6					1					2									3	43
Erythromycin	2 64 wk	10		2	7	1																	0	0
Novobiocin	12 wk	1			1																		0	0
Oxytetracycline	1 85 wk	13		8	4	1			6		1			1					1				9	69
Potassium Penicillin	2 days to 110 wk	22		10	8	4			2				1								1		4	18
Phenoxymethyl penicillin	2 8 wk	7		2	3	2																	0	0
Phenoxymethyl penicillin K	2 days to 8 wk	15		7	6	2										1							1	7
Tetracycline hydrochloride	5 days to 321 wk	60	4	42	14		1	1	2	1		1		1	1		1		2				9	15
Tetracycline phosphate buffered with citric acid	1 53 wk	3		3																			0	0
Tetracycline phosphate with nystatin	4 days to 109 wk	139	8	94	33	4					2		1	4		2		1		1	1	1	13	9
Tetracycline sodium metaphosphate with nystatin	2 5 wk	4		4																			0	0
Triacetyloleandomycin	4 days to 3 wk	5		3	2																		0	0
Sulfadimethoxine	1 11 wk	8		3	3	2																	0	0
Sulfisoxazole	1 40 wk	9		4	4	1							1								2		3	33
Totals		312	13	196	86	17	1	1	11	1	3	1	3	8	1	3	1	1	3	1	4	1	41	11

* Response excellent 91 100% improvement good 76 90% improvement fair 26 75% improvement poor 0 25% improvement

† Several patients experienced more than one side effect

Summary and Inferences

The results of therapy with a variety of orally administered antibiotic and sulfonamide drugs used in the management of acne vulgaris are reported Treatment was given to 208 patients with moderately severe to severe pustular and cystic acne or acne conglobata The duration of 312 courses of orally given therapy ranged from two days to six years and nine weeks in these patients Of these 312, the results were excellent in 13, good in 196, fair in 86, and poor in 17 Seventy-five patients received one or more of the antibacterial agents over more than six months Sixteen different antibiotic and sulfonamide drugs or modifications thereof were prescribed Twenty-seven patients had complaints which required discontinuation of the particular drugs Only six of these were unable to tolerate two or more of the medicaments tried In all except one patient, the side-effect occurred within 9 weeks after starting medication, in 43%, the side-effect occurred within 10 days

With the exception of one case of Candida albicans vaginitis, no serious side-effects attributable to these drugs were encountered, all minor complaints disappeared without difficulty within a few days after administration of the medicament was discontinued Furthermore, there were no instances of intercurrent infectious or other diseases which could be blamed on the prolonged administration of these agents The development of clinical resistance of the acne to these agents was exceptional and presented no serious clinical problem in management

999 Fifth Ave (28) (Dr Sulzberger and Dr Witten)

The tetracyline phosphate with nystatin (Comycin) was supplied by the Upjohn Company, Kalamazoo, Mich

The opinions herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large

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THE WELFARE STATE —We have been aware for some time that the shades of the Welfare State, like the shades of the prison-house in Wordsworth s ode, are beginning to close upon us, as upon the growing boy In fact, we have been aware that these shades may well materialize into shackles for us, as has happened to our confreres overseas So let us face the facts The Welfare State, for good or ill, is already here If we had any lingering doubts on this score, they were dispelled very bluntly recently by a senior member of Cabinet, who reminded us of this fact, and said there was little we could do about it Governments of late years have given up the frontal type of attack on the profession in favor of infiltration This can be very effectively carried on by the pernicious development of government by regulation The National Health Act lends itself admirably to this method of attack Dangerous regulations may be implemented this way —B A Cook An Address Thoughts of a New President (New South Wales Branch of the British Medical Association) *The Medical Journal of Australia,* June 4 1960

Zitowitz and Hardy[36] studied the influence of cold exposure on thermal burns in the rat They concluded that "exposure to cold reduces the burn severity and healing time if applied soon after the burn " They believed that "the cooling must be done early in the post-burn period, otherwise the effect of the reduced skin temperature is to increase the burn area and the healing time "

Stone and Martin[10] studied the effect of hypothermia in the dog A brief period of hypothermia during the initial treatment of the severely burned dog was well tolerated, and such a procedure was thought to be of considerable aid in the human being The metabolic rate was definitely lowered Through peripheral vasoconstriction, the loss of colloids, electrolytes, and fluid into the burned area was diminished During the first four to six hours there was only moderate alteration of blood-volume relationships, so that adequate time was available for colloid replacement The morbidity resulting from the burn was certainly not increased, and these studies indicate that it was actually diminished so long as hypothermia was not prolonged

Generalized hypothermia, as it is presently used in certain surgical procedures, is known to carry with it certain dangers which stem from reduction of cardiac output, inadequate respiration, and increased cardiac irritability It must be emphasized, however, that in this study no attempt was made to induce generalized hypothermia The most severe burn cases in this group involved body areas of less than 20% of the total body surface

Monitoring of oral temperatures revealed no lowering of such temperatures in almost all cases Only in the occasional patient did the body temperature drop, and then to not less than 97 6 F (36 4 C) In fact, on numerous occasions hot drinks have been given to the patients undergoing ice-water treatment, to offset any subjective feeling of generalized chilling while at the same time maintaining local cooling of the burned part

Moore[5] stated that local application of cold might be expected to reduce the fluid permeation, if the heat damage has left some reactive arterioles that can constrict He then stated that inadequate experience had been gained to make a solid conclusion on this point but that the experience recorded had been generally disappointing, save in localized burns However, it is reasonable to assume that some elements of first-degree and second-degree burns are almost invariably present in patients with severe third-degree burns Subcutaneous edema occurs in those areas as well as in areas with third-degree burns Diminution of subcutaneous fluid accumulation in that less severely damaged unknown fraction may alone be of sufficient value to make the difference in the "dangerous but salvageable" burn

The results of recent extensive experiments on rats by Ofeigsson,[1] in which cold-water treatment was applied to burns and compared with untreated controls, reveal a striking phenomenon which may explain some of the beneficial effects of cold-water treatment In the scalded areas of water-cooled tissues, "patches of almost normal skin could be found at any part (towards the periphery or centrally) although the intervening areas were more or less affected by the scald " In the control groups the damage was always uniform over the entire scalded area to begin with, and later became most marked at one point—usually in, or near, the center of the scalded area The "patchy" areas of less damaged tissue in the cold-water-treated animals may explain the better regeneration of these tissues when compared with the more uniform damage of the controls Another striking observation was the lesser degree of penetration of the burn damage in the treated animals when compared with the nontreated controls

Search of the literature reveals only scattered references to the cold-water or ice-water treatment of clinical burns The largest series was reported by Rose,[6] and his regimen proved to be almost identical with ours He suggested gradual warming of the water in the second and third hour of treatment, and in this period morphine was given for pain We did not warm the water and have had practically no need for narcotics Rose also reported the use of this method in a small series of severely burned patients with over 50% body involvement, with resultant survival He further reported that the mortality had been reduced from about 16% before cold water treatment to 7% when the treatment was used Although the numbers reported are small (40 patients), these data suggest that, even in the most severe burn cases, the cold-water or ice water treatment may be a safe and beneficial form of therapy

While the value of this mode of therapy for patients with extensive burns in shock remains to be tested on a large scale, its merits for those with burns of lesser degree should not be doubted in the light of the above observations It is recommended that the ice-water treatment be tried in those centers where more severe burns are seen in great numbers and where adequate controls can be established for comparison with other modalities

Ice and some form of refrigeration are commonplace in the United States during all seasons and therefore easily available at all times It is suggested that this humane and simple form of first aid management of less extensive burns should find its way into the thousands of books, manuals, and pamphlets on first-aid throughout our nation

Conclusions

Immersion of burns in ice-water baths, or the application of ice-cold moist towels to burned areas is recommended as first-aid emergency management for burns involving less than 20% of the body surface The treatment is inexpensive, easily availab humane, and harmless There is evidence to suggest that this treatment suppresses the pathological chain of events that follows a burn

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FRACTURE OF THE MONTH, NO 2

Multiple Fractures and Dislocation of Ankle

Presentation of Case

Otto E Aufranc, M D, Boston

Dr D W Florence A 26-year-old telephone company supervisor, heavy in stature, was sitting in the right front seat of an automobile involved in an accident of considerable force The patient was unaware of the exact details of the accident because of a temporary phase of amnesia She was brought immediately to the Massachusetts General Hospital by ambulance, there was no treatment prior to her arrival in the emergency room

Her obvious injuries were closed fractures of the left tibia and fibula, with angulation, plus a dislocation of the right ankle (internal rotation and adduction), with loss of the dorsalis pedis and the posterior tibial pulses on the right The dislocation was immediately reduced without anesthesia, and both pulses promptly returned The malalignment of the left tibia was also adjusted with ease, and a pillow splint was applied The circulation, sensation, and motor power distal to the latter were all intact There was also a palpable closed fracture of the left clavicle at the junction of the middle and outer thirds Multiple abrasions and lacerations were also present. X-ray examination confirmed the oblique fracture of the left tibia at the junction of the middle and lower thirds, with a transverse fibular fracture at the same level (Fig 1 and 2) No fractures were seen in the right ankle, and no ligamentous laxity was observed on stress films The left clavicular fracture was slightly displaced The patient's general health had been good, and there were no medical complications to the present condition The right ankle injury was treated initially with a splint and eventually with a short leg cast and elevation A thin sandbag was placed between the scapulae to reduce and maintain the clavicular fracture

Discussion of Case

Dr E F Cave We are apparently dealing with an obese young woman who was temporarily amnesic and who suffered multiple injuries, the obvious ones being a fracture of both bones of the left leg, a severe fracture dislocation of the right ankle with circulatory disturbance of the foot, a fracture of the left clavicle, and multiple lacerations and bruises We must assume that they were the only injuries present However, any patient who has received multiple severe injuries deserves an extremely careful examination immediately after arrival in the emergency ward The degree of shock must be evaluated and adequately treated, and a careful examination of the chest and abdomen must be performed Possible injuries in order of frequency in the abdomen would be trauma to the kidney, spleen, liver, and bowel It is assumed that these possibilities were ruled out as were any serious injuries to the rib cage and its contents

We are to discuss only the closed fracture of the midshaft of both bones of the left leg I am not entirely content with the films of the tibia and fibula, which suggest that there is some comminution that is not evident in the relatively poor film I should prefer films of better detail in antero-

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From the Massachusetts General Hospital

posterior, lateral, and oblique views The fracture of the tibia is apparently moderately oblique, possibly comminuted, and that of the fibula more transverse Adequate clinical examination and films of questionable areas should be taken, and appropriate treatment should be carried out

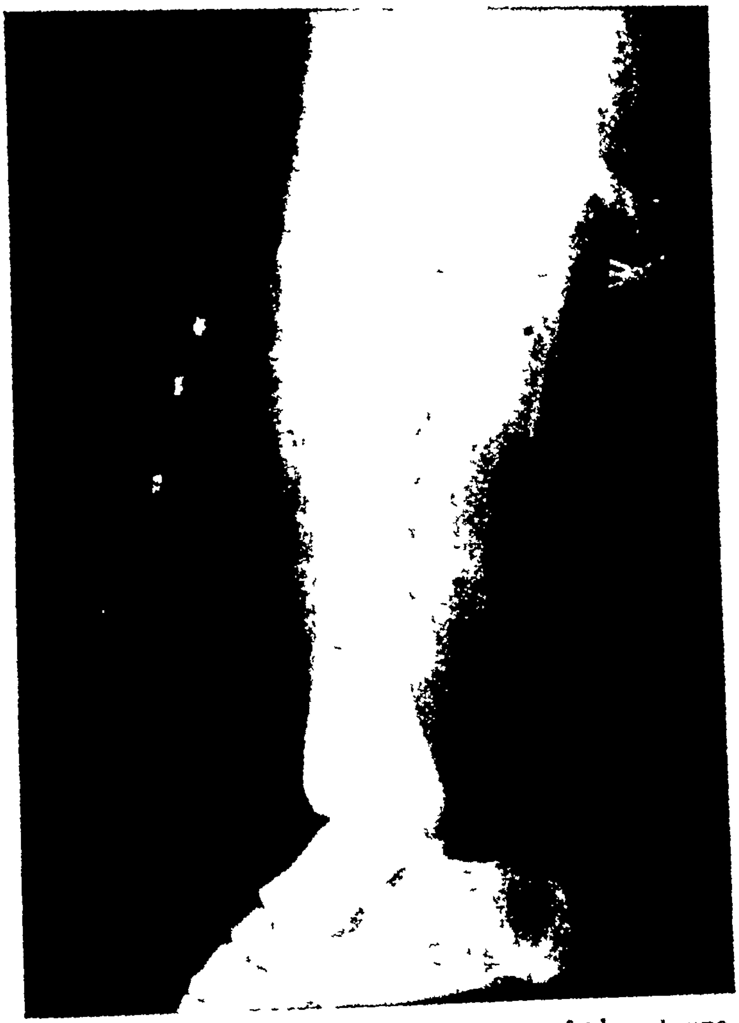

Fig 1 —Lateral view of oblique fracture of tibia at junction of middle and lower thirds taken shortly after patient's admission

A pillow and side splint was applied This is an excellent form of splinting for temporary care of the fracture Very often one will find that this type of immobilization will maintain effective reduction extremely well for a long period of time However, it is a clumsy type of apparatus Consequently, if one is to attempt closed methods for treatment of this fracture, one must use some other form of fixation, preferably plaster of Paris For the very short, oblique fracture of the tibia and the more or less transverse fracture of the fibula, I believe the surgeon would be justified in first trying a closed manipulation of this fracture, with the hope of locking the fibular fracture, and, in so doing, realign the tibia satisfactorily in order that it might be maintained in plaster I would administer a general anesthetic to this patient The objection to trying a closed maneuver in this patient is the fact that she is obese, and applying a plaster cast to an extremely fat leg is difficult With an unstable fracture it may not be possible to maintain the position

If the manipulation is carried out, portable x-ray films should be taken to determine whether the position is reasonably stable If it is, plaster of Paris should be applied, with only one layer of padding, with the knee flexed 30° to 40°, and with the foot in a position which would give the greatest stability to the fracture of the tibia An equinus position for three weeks will not do harm, if such a position is required Following the manipulation and plaster application, x-ray films should be taken in 24 hours and every other day for at least a week, if necessary, to determine whether the position will be maintained

Displacement and shortening of ⅜ inch and angulation of 10° of the tibial fracture would indicate that the closed method of handling the injury would not succeed If this occurs, I would proceed with some form of open treatment My choice for the open method would be that of application of a plate and 4 screws, the plate being applied to the lateral aspect of the tibia I believe also that the application of an osteoperiosteal graft, removed from the proximal fragment of the tibia and placed over the posterolateral aspect of the bone, tends to insure healing The fibula, of course, would not require internal fixation Wound closure should be carefully performed without tension, plaster applied with the knee flexed at 30° to 40°, and th foot in a neutral position The leg should be e vated subsequently until wound healing has o curred If temperature, pulse, and white blood count remain normal, if there is no undue pain

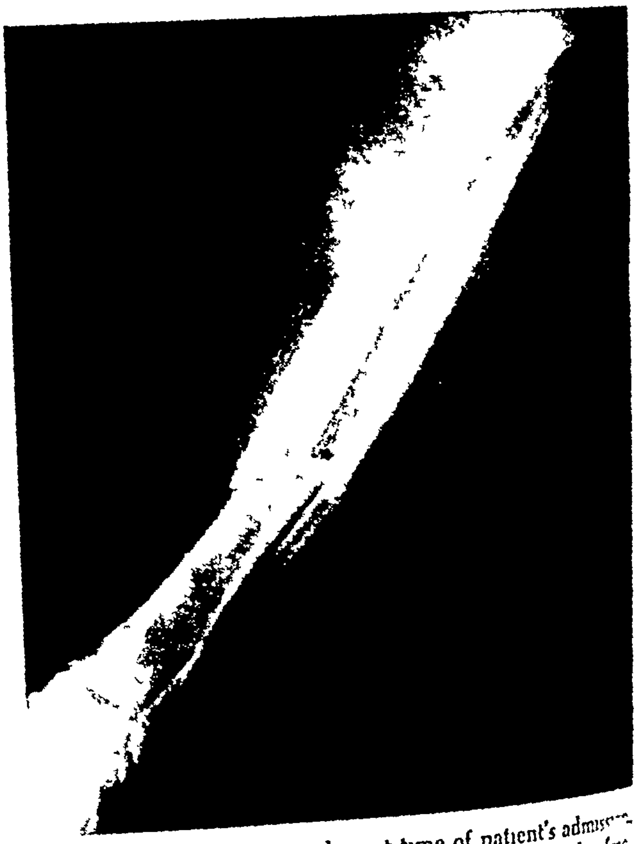

Fig 2 —Oblique view taken at time of patient's admis- showing oblique tibial fracture and transverse fibular frac ture at the same level

the fracture site, and if there is steadily diminishing swelling of the foot, one need not change the plaster until time for removal of stitches at the end of two to three weeks At that time a new plaster casing should be applied

As to other forms of internal fixation which might possibly be used, I suppose some of my colleagues would use the medullary (Lottes) nail I am personally not enthusiastic about the medullary nail for fractures of the tibia A nail tends to distract the fragments and sometimes comminutes the fracture, and I do not believe healing is as rapid with the medullary nail as with proper application of a plate and screws A medullary nail, however, would have the advantage of allowing earlier ambulation and weight bearing on the injured tibia and fibula than would the use of a plate and screws Other forms of internal fixation which might be used are the Rush or Steinmann pins, placed above and below the fracture and incorporated in the plaster The older method of treatment with skeletal traction by means of a Kirschner wire through the os calcis has largely been abandoned in our clinic because of the necessity of prolonged hospitalization and a tendency to distract the fracture

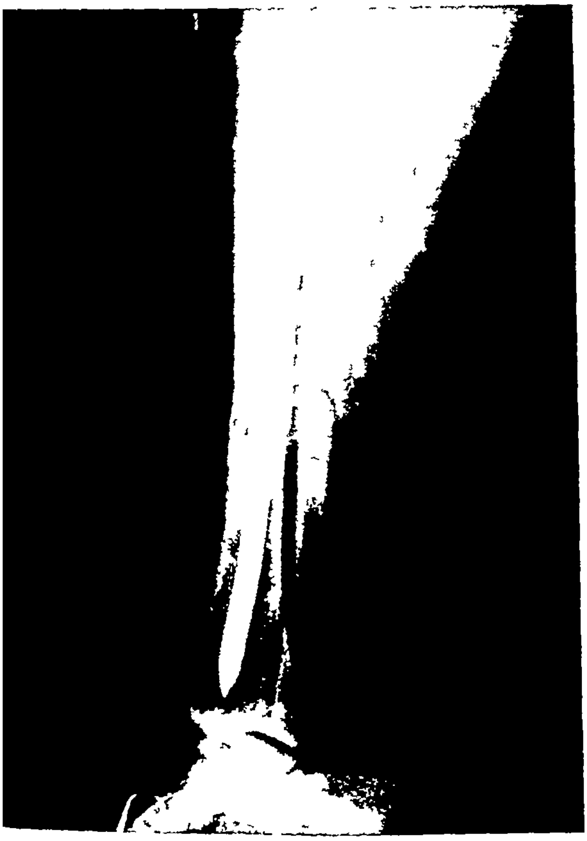

Fig 3 —Postoperative view after insertion of Lottes nail, showing closure of the fracture line of tibia

Fractures of the tibial shaft are notoriously slow in healing, and we must realize that open reduction of any form of a long bone fracture does delay healing, consequently, I should expect that postoperative immobilization would last five or six months Complete, uninterrupted plaster fixation must be carried out until healing of the bone occurs This can be determined only by examining carefully the x-ray films taken in anteroposterior, lateral, and oblique views

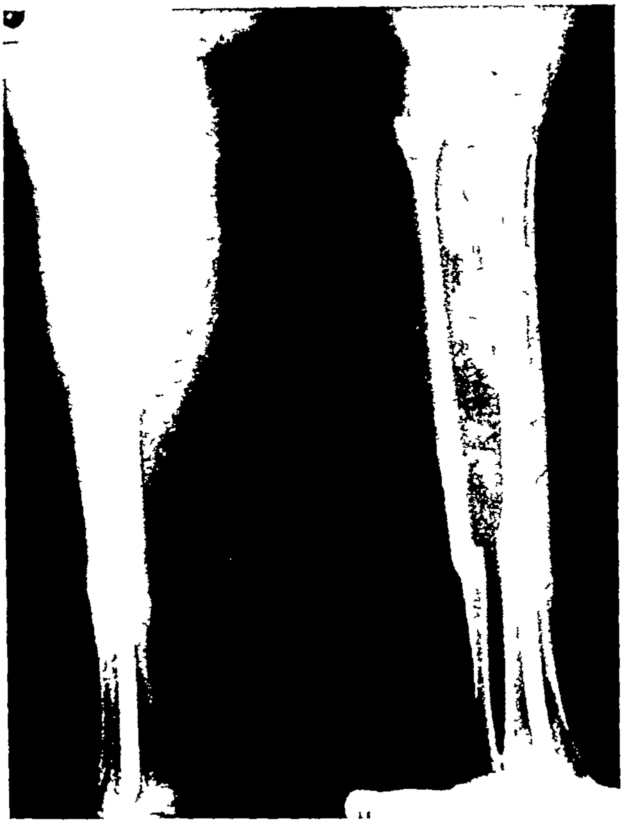

Fig 4 —X ray films taken 9 months after injury, showing excellent healing and obliteration of the fracture line

One would expect to see some evidence of healing of this fracture within six to eight weeks, and I would have no objection to the use of a long leg, walking plaster cast at the end of two months if there is evidence of progressive healing according to the x-ray films I find no place for the use of any brace in the treatment of this type of long bone fracture The leg must be immobilized in plaster until bone healing has occurred and until weight bearing can be allowed, with crutches They may be discarded when joint function and muscular strength return to the extremity and when the patient can walk without a limp

Dr W N Jones Though there is considerable deformity at the fracture site, this is largely rotatory, and closed treatment might be possible When displacement with overriding is apparent by initial x-ray examination, ordinarily there is little chance of maintaining what reduction can be achieved But in this particular fracture overriding is not present, and I would first attempt reduction *without* general anesthesia If the fracture is not obviously unstable on handling, a long leg cast probably would maintain reduction If the fracture does not feel stable, I would then employ open treatment, using a Lottes nail Minor comminution would not interfere with good stability

Dr D W Florence Because of the fairly good alignment seen in the initial x-ray films, a closed reduction was done, and a long leg cast was applied, with the knee flexed 35° In the process of applying the cast, with the patient under general anesthesia, it was obvious that accurate control of the fracture fragments was impossible because of the amount of fat in the leg

Because of the loss of alignment and overriding, a 13½ inch Lottes nail was used in the open reduction, which was performed 14 hours after admission The result is seen in Figure 3 This was done through a bayonet type of incision over the fracture site, plus a separate longitudinal incision just medial to the tibial tubercle An attempt at "blind nailing" (insertion of the nail without opening the fracture site) was attempted but was not successful Stable fixation was obtained, in spite of a 3-inch crack in the anterior portion of the cortex at the insertion site A long leg cast was applied postoperatively, and constant elevation was maintained

Although the incision over the fracture site was closed, with a fair amount of tension, healing was uneventful and without complication Both operative wounds were observed through windows in the cast, and all sutures were removed on the 11th postoperative day Eighteen days postoperatively, a new long leg cast was applied when the patient complained of burning in the heel, however, no skin changes were found

Six weeks postoperatively, the cast was removed from the right leg, and ankle exercises were started At seven weeks a walker was applied to the left, long leg cast, and the patient began ambulation on crutches, with partial weight bearing on the left At nine weeks after injury, the left, long leg walking cast was reduced to a short leg walking cast, and the patient was using crutches when discharged Callus formation at that time was abundant The patient admitted later that she rarely used the crutches after her discharge

The plaster cast was removed three months after injury By six months the patient had full painless ranges of knee and ankle motion and union of the fractures demonstrated clinically and by x ray films She returned to her original job as telephone company supervisor, on her feet, six months after injury Figure 4 shows x-rays of the fractures taken at nine months, with the fracture lines obliterated The end-result classification of this fracture is as follows anatomically 4, economically 4, functionally 4 (rating explained on page 9 of "Fractures and Other Injuries")[1]

Dr O E Aufranc This fracture probably could have been managed by closed methods had we been satisfied with some overriding, shortening, and angulation, even within the limits set by Dr Cave The staff accepts the principle of attempting closed reduction in almost all long bone fractures However, the obesity of this leg was the major factor in the decision to do an open reduction of this fracture after one attempt at maintaining position by plaster

The hazards of operating through thick layers of fat must be considered, and consequently closure of the fat layers must be done carefully and dressings applied gently It seems reasonable that open reduction and some type of internal fixation is the treatment of choice in such a fracture in this type of patient A delay, as opposed to an immediate open reduction, does not compromise union In fact, there is some evidence to the contrary

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[1] Fractures and Other Injuries, edited by E F Cave, Chicago, The Year Book Publishers, Inc , 1958

DURATION OF HOSPITAL STAYS OF OLDER PATIENTS —At ages 60 and over, the hospital admission rate for men is appreciably greater than that for women, but the average duration of stay is much higher for the women When both the incidence of hospitalization and the average length of stay per case are taken into account, it is found that women utilize hospital service slightly more than the men do   Nearly two fifths of the total time that the men in this study spent in the hospital for nonsurgical conditions was for heart disease Men hospitalized for this disease stayed an average of 20 days, for coronary artery disease alone the average duration of hospitalization was only a little shorter The men admitted to hospitals for psychoneuroses and psychoses stayed an average of about 108 days—longer than for any other disease, surgical or nonsurgical Although psychoneuroses and psychoses accounted for only 3 percent of nonsurgical cases among men at ages 60 and over, these disorders were responsible for 17 percent of the time that men spent in the hospital for nonsurgical conditions —Hospitalization at the Older Ages, *Statistical Bulletin,* October, 1959

SPECIAL COMMUNICATION

Study of a Preceptor Program

John Z Bowers, M D, Madison, Wis and Horace A Page, Ph D, Philadelphia

During the past four years we have evaluated a preceptor program which has been required for all medical students at the University of Wisconsin since 1925 Opinions of alumni and students on a variety of items, a historical note, and restatement of the objectives and methods of the program based, in part, on our studies are included in this report

History

A preceptor is traditionally envisaged as a physician who gives a highly personal training to an undergraduate medical student The usual picture of a preceptor is that of a general practitioner in a rural setting with a student accompanying him in his manifold medical activities In earlier days the terms preceptorship and apprenticeship were used interchangeably to describe the predominant system of medical education in the United States From the founding of the colonies until the establishment of the first department of medicine at Philadelphia in 1765, medical schools in the old world or preceptorship training were the only avenues to medicine for the youth of the United States About 90% of the practitioners in the United States were products of preceptorships copied rather poorly from the apprenticeships of England and Scotland Although these were seven years in length, programs in the United States were usually only three years

With the establishment of medical schools in the United States during the latter part of the 18th century, there was a fusion of formal instruction with a period of preceptorship However, the medical school was considered to supplement but not supersede the preceptorship [1]

The more eminent practitioners frequently had preceptorial classes of several students, and, in return for students services, lectures and quizzes were offered as regularly as in college Thus, in sequence, a youth of 16 years of age would serve a three to five year preceptorship, take a course of lectures at a college and receive the degree of Bachelor of Medicine, spend three more years with the preceptor, and return to the college for a second course of lectures, preparation of a thesis, and the award of an M D degree

As the population burgeoned after the Revolutionary War, medical education declined rapidly in quality Any youth who could read and write a bit and, most important, pay the fee might be accepted as indentured labor in a physician's office In many instances affiliation with a formal medical school program disappeared Fortunately, a scattering of physicians continued to plead for an upgrading of preceptorships In 1850 the Medical Association of the District of Columbia resolved that "no member shall receive into his office for preceptorship a student without a certificate of good moral character, a good English education that he is well acquainted with the elementary principles of mechanics, optics, acoustics, pneumatics and hydraulics, the elementary methematical sciences and a competent knowledge of Latin and Greek " [2]

In 1832, Daniel Drake listed the following desirable qualities of preceptors sound and discriminating judgment, learned, at least in his profession, devoted to his profession, jealous of its character, ambitious of its honors, conscientious in the performance of his duties, a man of business—punctual, accurate, and systematic, and of sound morals and chastened habits [3]

In many situations, although a medical student might register in a physician s office, he no longer read his books, accompanied him on his house calls, or attended in the office Medical education was carried on increasingly in the medical schools Those characteristics of preceptorships which were admirable disappeared to be replaced by didacticism and passivity

The Flexner report brought preceptorships to an end Save for a few institutions where students spent irregular periods observing in physician's offices, there were no preceptor programs in the United States until 1925, when the new four year medical school at the University of Wisconsin initiated a preceptor program [4]

In 1955, the Council on Medical Education and Hospitals of the American Medical Association reported that 24 medical schools in the United States offered preceptor programs These were required

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Dean and Professor of Medicine University of Wisconsin Medical School (Dr Bowers) and Associate Professor of Psychology Temple University (Dr Page)

in 10 schools and elective in the remainder The length of the programs varied from two weeks to four and one-half months In 80% of the schools, the preceptorship was offered in the fourth year The most frequent objective was to afford students an opportunity to observe medical practice in action[5]

The Wisconsin Program

The University of Wisconsin Medical School is situated in Madison, which had a population of about 25,000 people when the four year school opened There were no significant indigent groups available as teaching material Dr Charles Bardeen, who at that time was dean of the medical school, recognized two fundamental components of medical education He felt that the first of these, the science of medicine, should be taught by medical scientists in university medical centers The second, the art of medicine, should be taught by practicing physicians (The art of medicine was considered to be the methodology by which medical science is applied in practice) Accordingly, he selected a group of well established physicians and surgeons and asked them to gather either formal or informal groups of physicians to whom senior medical students would be assigned He suggested that the various specialties be represented and did not emphasize the need for general practitioners Thus, from the beginning, the program has centered primarily around men who were practicing medical specialties The reason for establishing the program is best expressed in Bardeen's words He said that it was created to "give the average undergraduate student an opportunity to learn something of medicine as an art through close association with a series of preceptors selected because of their skill in applying the science of medicine in daily practice "[6]

TABLE 1 —*Comments Regarding Preceptorship Program*

Favorable Comments	Percentage of Interviews in which Comment Occurred
Opportunity for contact with acute disease	100%
Opportunity for contact with specialty (or specialties)*	89%
Good instruction	72%
Emergency experience	69%
Provides student with experience with responsibility	45%
Opportunity to work in doctor's office	42%
Freedom in choosing activities	31%
Helps student to plan future more realistically	27%
Congenial atmosphere in which to learn	25%
Unfavorable Comments	
Limited program in specialty or specialties	42%
Insufficient responsibility	34%
Teaching inadequate or inferior	26%
Too much work assigned	25%

* Surgery, internal medicine, obstetrics, and pediatrics were mentioned more frequently than specialties such as neurology, pathology, and radiology This coincided with their order of emphasis in the preceptor program

From the beginning, the program has occupied three months of the fourth year The preceptorships are located in communities, varying in population from 500 to 500,000 Students are assigned singly or in pairs Of the 15 centers, 8 are directed by surgeons, 5 by internists, and 2 by general practitioners There are eight formally organized clinics that have staffs of 5 to 25 physicians and seven informal groups of 2 to 7 physicians These latter groups are gathered solely for educational purposes The number of house calls varies greatly Contact between the preceptors and the medical center is maintained by semi-annual meetings at the medical center and by annual faculty visits Students submit reports on their preceptorships, and from these reports information is gathered and transmitted to the preceptors

Attitude of Alumni—Two hundred graduates of the classes of 1932, 1937, 1947 and 1952 responded to questionnaires on the preceptor program[7] The preceptor program influenced the choice of internship or residency in 34% of the alumni who were interrogated The fact that only 13% were influenced toward general practice and 9% toward a rural area for practice may be attributed to the lack of emphasis on general practice or on rural areas in a majority of the preceptorships

The opportunity for contact with acute medical problems and the close teacher-student relationship were cited as the outstanding features of the program by over one-half of the alumni A wide variety of diseases was also considered to be a major attribute of the program Those alumni who had been practicing in a rural setting emphasized the value of the preceptorship as it afforded contact with acute medical and surgical problems This supports the general belief that the physician in rural practice is primarily concerned with the skills required to handle acute medical and surgical problems Criticism of the preceptor program was voiced by about one-tenth of the alumni Primary criticisms were that the preceptor was too busy to teach and that there was too much routine or too little responsibility As the number of years in the practice of medicine by these alumni increased, the preceptorship was more strongly endorsed as an important educational experience

Attitude of Students—Student reactions to the program have been gathered through interviews and questionnaires, the classes of 1957 and 1958 totaled 151 students (table 1) These were administered before and after the preceptor experience

The most frequent favorable comment was that the students had an opportunity to see "a different type of patient and wider range of disease than we see in the University Hospitals" In assessing the significance of this statement, it must be understood that the University of Wisconsin Hospitals admit patients who are primarily complex diagnostic and therapeutic problems Cancer and degenerative diseases are the major problems Although medical educators emphasize the fact that the procedures for a history and physical examination can be learned from any type of patient, our studies re-emphasize the fact that students are eager for contact with a wide variety of medical problems

Comparison of Preceptor Program with Fourth-Year Clerkships—In one of our studies, fourth-year students of the class of 1958 were asked to compare the preceptorship with the clerkship programs at the University Hospitals (table 2) As in our other studies, the opportunity for contact with acute illness, student responsibility, close teacher-student relationships, opportunity to learn a great deal about handling patients, and increased confidence of the student in his role were the characteristics considered most favorable

Student Self-Appraisal and the Preceptorship Program—We have studied the changes in student self appraisal in relation to preceptorships and other programs of the fourth year Questionnaires were given in October to students who had completed the preceptorial assignment and to those who had completed assignments on obstetrics, pediatrics, and neurology In January, students who had completed medical, surgical, and preceptorship assignments and classmates who had completed all fourth year programs except the preceptorship received questionnaires These comparisons for the class of 1958 were averaged together and are presented in table 3 Students rated themselves along a scale ranging from the ability associated with an average third year medical student to that of an experienced physician Lower scores indicate that a greater degree of skill or ability has been assigned Students who had completed the preceptorships had more favorable mean self-ratings on all the items except that dealing with diagnostic ability Statistically, significant differences favoring the preceptorship were noted for therapeutic skill and ability to handle emergency work

TABLE 2—*Student Ratings of the Preceptorship Compared With Fourth Year Clerkships*

Characteristic Rated	Preceptorship	Fourth Year Programs[*]			
		A	B	C	D
Provides an opportunity for considerable learning	1 8[†]	1 6	1 9	2 7	2 0
Leaves the student feeling more confident of his role	1 6	2 2	2 1	3 2	2 1
Program where the student can learn a lot about handling patients	1 7	2 4	1 7	2 9	2 4
Program characterized by close teacher student relationship	1 6	2 4	2 2	3 3	2 2
Program distinguished by fine instruction	2 4	1 8	2 0	3 2	1 8
Program where the student is given responsibility	2 3	2 9	1 7	3 6	2 9
Provides contact with acute illness	1 3	3 4	2 8	3 2	2 [illegible]
Program which is popular with students	1 5	3 4	2 8	3 2	2 6

[*] Statistically significant differences were noted among the various programs for each of the ratings

[†] Fourth year students made these ratings at the conclusion of the year and after they had participated in all the programs noted above Items were rated in terms of the frequency with which a particular characteristic could be applied to the program under consideration Lower scores indicate more desirable ratings

TABLE 3—*Comparison of Self-Ratings of Ability of Students Who Had Completed the Preceptorships with Those Who Had Not (Class of 1958)*

Nature of Rating	Preceptorship Students[*]	Nonpreceptorship Students
Ability to establish rapport	2 35[†]	2 42
Therapeutic skill	3 49	3 80[‡]
Sensitivity to psychological and social problems	2 44	2 60
Ability to accept responsibility	3 11	3 24
Diagnostic ability	3 38	3 33
Ability to handle emergency work	3 41	3 86[§]
Maintenance of proper degree of detachment from patients	2 95	3 09

[*] In these comparisons, 37 fourth year students were included in the preceptorship group and 35 in the nonpreceptorship group

[†] Lower ratings numerically indicate more favorable self-rating

[‡] Significance at the 0 05 level

[§] Significance at the 0 01 level

Since the preceptorships are likely to provide the student with the first opportunity to see emergency medical problems, the higher rating in this area is not surprising The self-evaluation of diagnostic skill presents a more difficult problem in interpretation It is not clear whether this can be attributed to greater confidence among students who have remained at the University Hospitals or a decrease in confidence in students who have seen difficult diagnostic problems away from the teaching hospital Students who had been assigned to preceptorships which were generally accorded a favorable student evaluation were more likely to show more positive self-evaluations than those who had been assigned to less favorably regarded preceptorships Within the limits of these observations, it appears that the preceptorship does result in changes in the way students tend to regard themselves These changes seem to be largely related to the indoctrination by fire' kind of experience which is more likely to be afforded by the preceptorship than it is by the programs at the teaching hospital

Student Career Plans—In an effort to determine the effect of the preceptorship on subsequent type of practice, we studied career decisions among third and fourth year medical students Fifty-two per cent of a third year class indicated general practice as their first choice In the fourth year 56% of the postpreceptor group and 63% of the control group had made changes in their choices These were primarily toward general practice, usually in association with a small clinic group We were impressed with the high percentage of students reporting an interest in general practice It is evident that many medical schools produce a graduate who is sincerely interested in general practice Associations during the internship play a more significant role in the swing toward specialty practice than critics of medical education are willing to admit

The classes of 1957 and 1958 were studied for changes in career plans which were influenced by the experience of the preceptorship Thirty-six per cent of the postpreceptorship group indicated change in career plans, and 38% of the students on University Hospital clerkships made similar changes over a comparable period of time In both groups, the change was from specialty practice to general practice The percentage of students changing from general practice to specialty practice was also essentially the same in the two groups Thus, there was no effect of the preceptorships on career plans Similarly, no systematic changes were noted with respect to such decisions as type of internship or group versus individual practice which could be associated with the experience of the preceptorship Students' plans varied in many cases, but these changes would appear to have been dictated by any number of factors

Evaluation of Students by Preceptors and by Medical School Faculty—We were interested that the preceptors' ratings of students correlated positively with the Physicians' Scale of the Strong Vocational Interest Inventory ($r = 0\ 38$, $P < 0\ 01$) and with averaged scores from the National Board Examination ($r = 0\ 506$, $P < 0\ 01$) The preceptors' evaluations bore only a negligible relationship to the students' grade point averages at the medical school ($r = 0\ 204$, $P < 0\ 05$) We have compared grades by medical school faculty, grades by preceptors, and results on the National Board Examination, part 2 Students whose National Board performance was below that which would be expected from medical school grades were designated as "over-achievers," while those whose National Board scores were higher than grades would predict were called "under-achievers" Typically, the "over-achievers" were described by their preceptors as eager, hard-working, frank, forceful, and efficient students, while the "under-achievers" were more likely to be seen as sympathetic and sincere people The performance ratings of both types did not differ significantly, but the "over-achievers" were more likely to be described by the preceptors as well suited for specialty practice The "under-achievers" were more confident of their abilities than the "over-achievers" were While the "over-achievers" were more critical of the preceptorship program than were the "under-achievers," they tended to be more positive in their evaluation of the total medical school program

Unfavorable Student Attitudes—Twenty-nine per cent of the 1957 four year class felt that the preceptorships had an excess of routine responsibility and a lack of opportunity for study A similar percentage felt that they had not been sufficiently informed on schedule and responsibilities Some of the students with the best academic records felt that the preceptorship was too much like an internship

Implications—Our studies were carried out in part because of the strong feelings, both pro and con, that exist in regard to preceptor programs We believe that in the setting of the University of Wisconsin Medical School the preceptor program makes a valuable contribution to the total educational effort A medical school in a large metropolitan area with a wide selection of medical problems including acute disease, a busy outpatient program, and an active emergency service would probably have a very different attitude about preceptorships Perhaps other medical schools in a setting similar to that of Wisconsin would find a preceptor program of educational value

Restatement of Objectives and Methods—The knowledge gathered from our studies has been helpful in reviewing and revising the preceptor program A committee of preceptors and members of the full-time faculty has prepared the following program which has been adopted as our present pattern We suggest that this program should receive the careful attention of any medical school which is considering a preceptor program

The Preceptor Program—Objectives and Methods—1960

Objectives—The preceptor program is an integral and important part of the medical school curriculum The primary objective is to enrich the academic experience of the fourth-year medical student by affording him the opportunity to (1) study acute medical problems and ambulatory patients, (2) evaluate social, economic, and environmental factors in disease through a close association with patients and their families, and (3) develop a personal working relationship with one or a few physicians

Methods—In order to achieve the primary objective, the guiding principle will be *to obtain the highest quality of academic experience available without regard to other considerations* No attempt will be made to obtain uniformity nor to cover all aspects of the practice of medicine Each preceptorship will develop a program which is representative of the interests of the preceptor and a few enthusiastic and qualified associates Thus, several types of preceptorships will be available, ranging from general practice to highly specialized group clinic practice An attempt will be made to match the students' interests and abilities with the particular program offered

The preceptor will be requested to review the current program in order to (1) determine the area or areas of academic endeavor best suited to the group, taking into account the quality of instruction and physical facilities available, (2) limit the number of associate preceptors to those who are academically qualified and who actively participate in teaching, and (3) provide the office of the dean of the medical school with detailed information concerning the program developed, physical facilities, and personnel

The student is directly and fully responsible to the preceptor His program and responsibilities will be discussed with him at the beginning of his preceptorship The work load of the student should be related to the educational opportunities afforded by a few carefully studied cases rather than a large number of cursory examinations Adequate time should be provided for discussion of his work with the preceptor

The preceptor is directly responsible to the office of the dean of the medical school and is requested to file an annual report citing the achievements, problems, and recommendations for changes in his program He is also expected to attend the semiannual conferences at the medical school Appointments of preceptors and associate preceptors will be reviewed on an annual basis Only those persons actively engaged in teaching will be listed in the medical school catalogue

The dean s office will arrange for periodic visits by faculty members to the preceptorships for the purpose of coordinating local educational objectives and practices with those prevailing in the medical school Students who have a solid on-going research program or a unique educational opportunity away from the medical school may, in carefully selected cases, be permitted to pursue either of these objectives in lieu of a preceptorship

418 N Randall (6) (Dr Bowers)

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DIGITALIS INTOXICATION —The increased sensitivity of primary hypokalemic states to digitalis is well established The ability of potassium to suppress arrhythmias and to correct digitalis intoxication is also well known The relationship between potassium and digitalis at the level of the myocardial cell remains indistinct, although digitalis effects are associated with potassium migration across the cell boundary Whether digitalis depletes cellular potassium or interferes with active transport of potassium into the cell has not been determined It is generally agreed, however, that digitalis overdosage causes intracellular potassium depletion, the severity of the reaction being roughly proportional to the extent of the overdosage Most instances of digitalis toxicity are unrelated to primary potassium effects but are associated with accidental overdosage or well-intended but unrealistic digitalization and maintenance regimens The proper dose of digitalis is always an individual pharmacologic experiment necessitating constant monitoring of clinical and electrocardiographic alterations Adherence to presribed routines unrelated to size or clinical condition of the patient is perhaps the most frequent cause of digitalis intoxication Other instances of digitalis intoxication may be related to communication difficulties between physician and patient The physician must insure that neither his own semantic difficulties nor the patient s lack of attentiveness or comprehension are permitted to interfere with proper instruction in the use of this potentially hazardous drug Perhaps of equal importance is careful education of patients in the early signs of overdigitalization The physician himself should recognize early clinical and electrocardiographic signs of digitalis intoxication —Major R H Moser M D Back-Door Digitalis Intoxication Review and Report of a Case, U S *Armed Forces Medical Journal*, April 1960

THE JOURNAL
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IRRADIATION OF THE HUMAN FETAL THYROID GLAND FROM I^{131} FALLOUT

THE law of Bergonie and Tribondeau,[1] applied to the production of thyroid cancer or hypothyroidism by irradiation, would suggest that thyroid abnormality could be produced in the fetal thyroid gland by a smaller dose of irradiation than is necessary in the infant or child Similarly, a smaller dose of irradiation would be required in the child than in the adult The communication Radioactive Iodine Concentration in the Human Fetal Thyroid Gland from Fallout' appearing in this issue of THE JOURNAL, p 1895, pertinently reports for the first time the detection of I^{131} in the human fetal thyroid gland from radioactive fallout

In 1950, Duffy and Fitzgerald [2] reported 28 cases of carcinoma of the thyroid gland in children under 18 years of age and found that 10 of them had received irradiation to the thymus in infancy Since then, over 114 cases of thyroid cancer have been reported in children who have had previous x-ray therapy in early childhood to the thymus, neck, or head areas for benign conditions The latent period between irradiation and the development of thyroid cancer has often been under 10 years Some authorities believe that the association between thyroid cancer and external irradiation to the head, neck, or upper chest in infancy must now be regarded as well established On the other hand, it is doubtful whether irradiation in adult life for the treatment of thyrotoxicosis, as discussed by Hammonds and associates in this issue (p 1902), predisposes to the development of a thyroid carcinoma

Clark found that the usual dose of externally applied radiation to the neck area of infants and children who later developed thyroid cancer was 200 to 725 r The estimated average dose to the human adult thyroid from radioiodine during the heavy fallout period of January, 1955 to December, 1956 was less than 0 04 rep Although these studies indicate that the I^{131} concentration in thyroids of children and adults is insufficient to deliver enough irradiation to produce hypothyroidism or thyroid carcinoma, no reports have been made to date on the detection of I^{131} from fallout in the human fetal thyroid gland The report in this issue of THE JOURNAL, stating that I^{131} does gain entrance to the human fetal thyroid gland from fallout to the mother, is of importance because there are at least four possible reasons why the concentration of I^{131} in the fetal thyroid and the irradiation effects of this I^{131} on the fetal thyroid might be considerably greater than in the adult thyroid gland

1 If the mother's thyroid gland were unable to concentrate I^{131} normally for any reason (i e, hypothyroidism or the ingestion of desiccated thyroid), the relative proportion of I^{131} taken in by the mother from fallout and available to the fetus would be increased

2 The placenta has been found in animals to be capable of concentrating iodine by a factor of four on the fetal side of the circulation

3 Small quantities of I^{131} in the fetal circulation would constitute relatively large quantities of I^{131} to the first few developing cells of the fetal thyroid because of the relatively tiny thyroid gland mass

4 These younger thyroid cells would be expected to be more sensitive to irradiation than the thyroid cells of even the infant or child

In view of these considerations, it is reassuring to read in the present report that, although I^{131} was found in the thyroid gland of the fetus, there is no evidence that the quantity of irradiation delivered to the human fetal thyroid gland was sufficient to produce hypothyroidism or thyroid cancer It would be even more reassuring, however, to follow living siblings of these fetuses, who were conceived during periods of more sustained fallout I^{131} concentrations, for periods of 10 to 15 years, to make certain that hypothyroidism or thyroid cancer did not develop later in life

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PRECEPTORS—TO BE OR NOT TO BE

The very sight of the word "preceptor" may elicit cries of anguish or odes of approbation from the medical educators who read the J A M A For this reason, if for no other, the reactions to the report on a preceptor program which appears in this issue of THE JOURNAL, p 1923, will be interesting and, we hope, will be communicated to us

The opponents of preceptor programs criticize the nonacademic environment, the lack of supervision, and the tendency to use medical students as "slave labor " The proponents emphasize the value of acquaintance with the actual practice of medicine, of recruitment for general practice in rural areas, and improved relations between the medical profession and the medical schools

The communication suggests that there are situations in which, because of policies and geographic locations, a medical school may find a preceptor program of essential value in expanding and diversifying the supply of teaching material The impending rapid expansion of facilities for medical education should result in a reappraisal of the role of preceptor programs We trust that this report will serve as a useful document for such discussions—and may the best plan win!

ORAL POLIO VACCINE

In 1950, Koprowski, Jervis, and Norton[1] discovered that the oral administration of a rodent-adapted laboratory strain of Type 2 poliovirus (the TN strain) to 20 non-immune children caused asymptomatic intestinal infection followed by the development of homotypic antibodies in blood In 1960, reports presented at the Fourth Scientific Conference and International Symposium on Live Poliovirus Vaccines held in Moscow in May[2] and at the Second International Conference on Live Poliovirus Vaccines held in Washington, D C in June[3] disclosed that about 60 million people have been fed the attenuated live poliovirus vaccines in many parts of the world

These mass vaccination programs have been preceded by a preparatory period of laboratory, clinical, and epidemiologic studies performed in a series of small, well-controlled trials in children and adults in the United States Paradoxically enough, the "jump" from these limited studies to trials of national magnitude did not take place in the U S but in the Belgian Congo in 1957, and from this starting point, vaccination on a large scale has been carried out in Africa, Asia, Europe, and South America

Critics of live virus vaccination programs consider small-scale trials epidemiologically inadequate to prove safety and efficacy and large-scale trials inaccurate because of the difficulty of maintaining close clinical surveillance The study reported in this issue of THE JOURNAL, p 1883, seems to bridge the gap between small preliminary studies and mass vaccination programs Eight hundred and fifty infants and children in well-baby clinics in two wards of Philadelphia were fed poliovirus vaccine This study was carried out in a quiet manner, without accompanying publicity, and it has shown every promise of effectiveness of the oral vaccine It is hoped that the portion of the population which has been reluctant to receive inactivated virus vaccine by injection may willingly submit itself to feeding, with the attenuated live virus No clinically discernible complication followed administration of the vaccine, and antibodies of the three types of poliovirus developed in more than 90% of the susceptible vaccinated children It should be noted, however, that the vaccine strains were administered separately at one-month intervals This is the first example of a cooperative trial of live virus vaccines, since Koprowski's Types 1 and 3 and Sabin's Type 2 strains were used in this study

Although the protagonists of live virus vaccination argue the superiority of one set of strains over another, differences between them are actually based on one type of test—neurovirulence for monkeys Apart from the fact that this test has no known correlation with pathogenicity for man, the recent detection of a contaminant, a so-called Simian virus, in batches of polio vaccines prepared from the three Sabin strains,[3] calls for the revaluation of the results of monkey neurovirulence tests In these tests, at least two viruses, one attenuated polio and one Simian non-polio, were injected simultaneously into monkeys As far as monkey neurovirulence is concerned, the results are questionable until new tests on poliovirus alone have been undertaken and evaluated

With the validity of the monkey neurovirulence test under question, one is left only with field experience in man as a basis for evaluating the safety and efficacy of the oral vaccines Here the simple count of millions is not sufficiently convincing The choice of a susceptible population, including the complete clinical and laboratory study of all post-vaccination paralytic cases, astuteness in the epidemiologic evaluation of the dissemination of the virus, and subsequent immunologic protection are only a few of the factors that should be considered in planning field trials A large-scale American trial is now called for, but the quality of scientific workmanship should not diminish in proportion to the increase in the quantity of subjects to be immunized

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RESPONSIBILITY FOR RECRUITMENT

The competition for talent in the professional schools in America is a fact of life that must be accepted by the physician in today's world This should not be a disheartening admission, rather, competition in this endeavor, as in many, should enhance the wits of the contenders and bring into sharp prospectus the ways and means of preventing dire consequences Of great concern at the moment is the need to attract a sufficient number of intellectually and emotionally qualified high school and college students to fill the ranks of the first year classes in our medical schools each Fall In so doing, we are obviously competing with the graduate schools of chemistry, physics, mathematics, engineering, and a myriad of others that are as interested in quality talent as are the admissions committees of the several medical schools

It is vital that there be a steady supply of apt, able, and mature college students who seek admission to medical schools Relaxation on the part of the physician, combined with a vigorous campaign of proselyting from many non-medical disciplines, is a cause of considerable concern This is the challenge presented to organized medicine and to the physician individually What is proposed to correct this grave situation?

Specific recommendations are pertinent in each category, i e, the American Medical Association and the physician The House of Delegates, at the 1959 interim session, instructed a special committee to design a scholarship program of which the A M A would be a major sponsor A follow-up report at the Miami Beach meeting held recently was reassuring The program will be helpful in filling each available berth in each medical school with predoctoral candidates of high intellectual caliber whose financial status should not be the stumbling block to a medical degree Each member of the American Medical Association contributes his pittance to this program But this is not sufficient If each physician in the United States were to assume responsibility for recruitment for medical school of one qualified student per year, our admissions committees would be in clover, an experience that has not been theirs for almost a decade Such a plan is practical and feasible and entails no financial subsidy The program should be a continuous one It requires no specific time for inception it should never end Summer is an excellent time to initiate it

The high school or college student should have no fear that his premedical training today requires the abandonment of a liberal education Quite the contrary The broadest possible liberal education, rather than a specialized one, is the prerequisite specifically defined by the medical schools I have a very selfish reason for urging premedical students to obtain as liberal an education as possible in the humanities generally and specifically in English and English composition More doctors are preparing more written communications than ever The results are sad in some instances as viewed by the Editor These are directly related to a deficiency of English composition in high school and college A liberal education should help to correct so obvious a void Almost as important is the development by the student, who is later to become a physician, of the urge to embrace good literature as an integral phase of his daily life If good reading habits are established before medical school, they may be suppressed temporarily during the formal years of training but will be recaptured thereafter It is similar to the acquisition of coordination in riding a bicycle

In some instances, the physician in his recruitment may need a dossier of directions or a prospectus for the potential candidate to peruse The American Medical Association has just published a kit on the subject[1] Also, R S Starrett has finished his monograph, "Find a Career in Medicine"[2] Starrett sought advice in the preparation of the monograph from Doctor Aura E Severinghaus, Associate Dean in charge of admissions at Columbia University College of Physicians and Surgeons, from Doctor Walter S Wiggins, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, and from several educators in the public schools in Evanston, Ill I suspect that, if it had been my responsibility to assemble the material, I would have de-emphasized the glamour of the operating room and emergency surgery The 1960 Doctor Kildare is more apt to be called by a walkie-talkie beeper than to hear his name blared out over the public address system These are minor quibbles Starrett presents a strong argument in support of the innumerable discoveries yet to be made in medicine and thereby emphasizes the challenges ahead for the new generation of doctors The discovery of a few wonder drugs, the prospect of obliterating poliomyelitis, and the eradication of malaria by public health means have not drawn down the curtain in the last act of research and medical progress In fact, we are probably in only the first act of the show The procedures and techniques in research and clinical investigation, which have been introduced in recent years, were not on the drawing boards of a Jules Verne or a Leonardo da Vinci when many of us were in medical school Many new devices not yet conceived will be available for the physician of the future These hard facts should be as challenging to the high school or college student as a trip to the moon Will you conduct a one-physician campaign to recruit one potential medical student per year?

J H T

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[1] The kit "Medical Careers" is available to physicians on request from the American Medical Association

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THE ARTHRITIC HOG

The gouty parakeet, the polyarthritic lamb, the osteoarthritic bull, the pulmonary osteoarthropathic pooch, and the arthritic hog, were discussed in a symposium held several months ago in Bethesda, Md on the comparative pathology of arthritis and rheumatism Dr Leon Sokoloff, Chief, Section on Rheumatic Diseases, Laboratory of Pathology and Histochemistry of the National Institute of Arthritis and Metabolic Diseases and Chairman of the sym posium, gathered together an outstanding group of avian and mammalian pathologists to review the studies that might contribute to our understanding of joint disease in humans Rudolf Virchow prophesied the importance of comparative pathology and urged that there be no dividing line between animal and human medicine Late in the last century, Theobald Smith reemphasized the importance of veterinary pathology in contributing to the solution of the problems of clinical medicine Sir Henry Dale, not more than a decade ago, affirmed that The problems of pre-clinical education in the two disciplines, medicine and veterinary medicine, are largely a matter of mutual interest and concern "

The proceedings of the symposium that have just been published[1] reveal the wide interest in this interdisciplinary approach to the study of joint disease Attention will be given only to two subjects that were discussed, which provide useful information in the investigation into the etiology and pathogenesis of rheumatoid arthritis in the human The hog is the vertebrate that has served as the subject of the naturally occurring malady as well as the experimental animal Theobald Smith isolated an organism from swine that resembled the causative agent of the malady rouget du porc (swine erysipelas and acute polyarthritis) He received a culture of the organism from Pasteur for comparative studies in epizootiology, (veterinary science, corresponding to *epidemic* as applied to diseases of man) The erysipelas bacillus has been isolated from the arthritic joints of market hogs Arthritis has also been induced in hogs by the intravenous inoculation of Erysipelothrix rhusiopathiae Rheumatoidlike arthritis in hogs continues to be a critical veterinary problem in this country According to the Meat Inspection Division of the United States Department of Agriculture, arthritis has ranked first, second, or third as a cause for condemnation of hog carcasses in recent years In fact, arthritis has superseded trichinosis at the present time as the major cause of condemnation

Clinical manifestations of the rheumatoidlike arthritis of swine include an acute process followed by chronic deforming changes in the joints The animal displays a critical pyrexia (106-108 F), with profound malaise and subcutaneous hemorrhages Extensive damage to the small blood vessels may be observed histologically Muscle soreness, tender feet, and symptoms of intra-articular involvement appear later Chronic arthritis with bulbous synovial villi, pannus formation, periostitis, and ankylosis are reported Gross inspection reveals lameness or incapacity Roentgenographic study shows osteophyte formation, with apparent ankylosis of the carpal and tarsal joints The articular processes of the vertebra appear to be fused Irregular ossification and rarefaction of the bones adjacent to the joints are observed

The Ery rhusiopathiae organism has been isolated from a number of animals These include fish, mud hens, blackbirds, turtle doves, white stork, herring gull, golden eagle, chipmunk, meadow mice, and the house fly Sensitization has been shown to be an intimate factor in the pathogenesis of the rheumatoidlike joint disease Hogs that have been vaccinated exhibit a marked anaphylactic reaction subsequent to an intravenous challenge dose of the same organism Allergens of the organism are capable of producing a lasting sensitivity A similar mechanism, hypersensitivity, has been postulated for the pathogenesis of rheumatoid arthritis in humans

The pleuropneumonialike organism (PPLO) is another microbiologic agent that has been isolated from arthritic hogs It will be recalled that Reiter's disease in man, a variant of rheumatoid arthritis, has been attributed, by some rheumatologists, to an infestation of a pleuropneumonialike organism Cultures from affected joints of pigs have been freed of bacteria of ordinary size by passage through a filter Propagation on embryonating chicken eggs may yield an active agent' that will produce a severe arthritis within a few days, when injected subcutaneously, intraperitoneally, or intra-articularly Microscopic examination of the articular exudates has failed to reveal bacteria, to account for the arthritis It has been concluded that the exudative reaction has been produced by an ultrafiltrable agent Although the arthritis is continuous, without remissions or exacerbations, it is not a strictly articular process A similar statement is applicable to some patients with Reiter s disease It is apparent that, serious though the problem of arthritis may be in man, the lower forms of animal life may share in the affliction, they may also contribute to our understanding of articular disease and thereby help toward solving the many unsolved problems of arthritis and rheumatism

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[1] Conference on Comparative Pathology of Arthritis and Rheumatism Lab Invest 8 1147 1498 (Nov Dec pt 1) 1959

THE ARTHRITIC AFFECTION, OR GOUT

Gout is divided into sciatica, and podagra, and ciragra and arthritica Indeed sciatica is arthritica of the hand, podagra is arthritica of the foot, and is like a type of lepra Some arthritica therefore arises from hot air which dissolves too much, or from the cold which constricts too much, from which the humors grow rheumy in the joints, or from frequent bathing, or from sojourning among those having repletion, or from much food and drink, or from frequent coitus after lunch —The Surgery of Theodoric, vol 2, books 3 and 4, translated by E Campbell M D, and J Colton, M A, New York, Appleton Century-Crofts, Inc, 1960, p 195 urethral distress, and (6) minimum expense of the anesthetic agent

Conclusion and Summary

The effective local anesthetic action of antihistaminic compounds for urethral anesthesia has been well established It is apparent that the antihistamines, particularly tripelennamine (Pyribenzamine) aqueous jelly 2%, are superior to other local anesthetic products

In a series of 738 male patients undergoing various urologic procedures tripelennamine aqueous jelly 2% proved to be an extremely reliable local anesthetic agent, no local or systemic reactions were encountered in the series Tripelennamine aqueous jelly 2% is recommended as a valuable clinical aid in the urological clinic

4867 Sunset Blvd (27)

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Sodium Dextrothyroxine and Sodium Levothyroxine

Results of Their Use in an Athyreotic Patient with Angina Pectoris and Hypercholesteremia

Paul Starr, M D , Los Angeles

It has been reported[1] that sodium dextrothyroxine (Dextroid) can reduce the serum cholesterol concentration in myxedematous patients in a dosage which does not raise the basal metabolic rate or potentiate the electrocardiogram Other studies[2] indicate that this drug lowers the serum cholesterol level in euthyroid idiopathic and diabetic hypercholesteremic patients Such effects might be due to the admixture of a small percentage of the levoisomer in the large amount of dextroisomer used in these patients, but the following case report makes this seem unlikely

Report of a Case

A 64-year-old woman had a total thyroidectomy in 1951 which resulted in athyreosis, indicated by a serum protein-bound iodine level of 1.6 mcg % and a 3% increase in radioactive iodine uptake after the administration of thyroid-stimulating hormone

Relief of myxedema was attempted, but the development of angina pectoris during the administration of desiccated thyroid necessitated a decrease in the dosage In 1958 (see figure), when the patient was given sodium levothyroxine (Synthroid sodium), 0.075 mg daily by mouth, the basal metabolic rate was —21% The pulse rate was 66 per minute, the blood pressure 220/100 mm Hg, and the serum cholesterol level 445 mg % Angina pectoris occurred frequently, even on this inadequate dosage, and necessitated the use of nitroglycerin several times a week Cardiac decompensation also occurred This was relieved by salt free diet and administration of chlorothiazide A decrease in weight from 140 to 110 lb (64 to 50 kg) occurred on this regimen

Sodium levothyroxine treatment was discontinued after an interval of combined medication and replaced by sodium dextrothyroxine given in a daily oral dosage of 4.0 mg In November, 1959, with the patient receiving this medication, the basal metabolic rate was +15%, pulse rate 58 per minute, blood pressure 230/110 mm Hg, body weight 110 lb, and serum cholesterol concentration 225 mg % Angina pectoris had not been experienced with the administration of this medicament during the eight months from April to December, 1959

To observe whether the cessation of angina pectoris was due to the change of medicament or to an improvement in the cardiac condition itself, the administration of sodium dextrothyroxine was, in turn, discontinued and replaced by that of sodium

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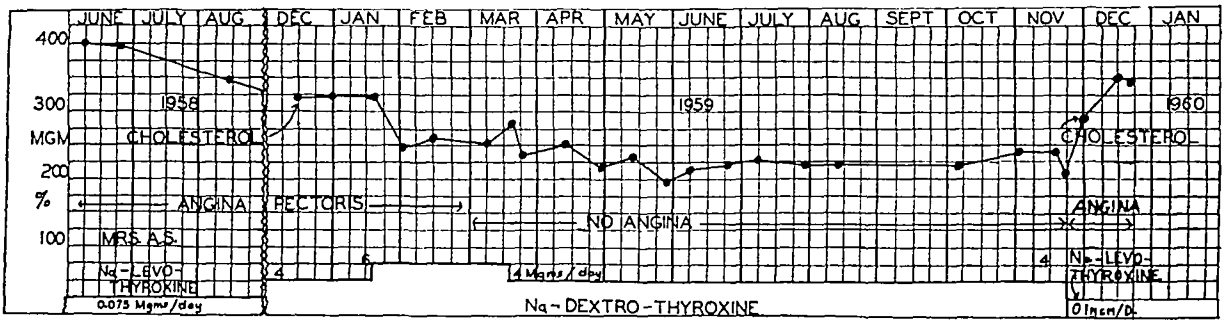
From the Los Angeles County Hospital

levothyroxine 0 1 mg daily Without change of weight or indication of cardiac decompensation, the basal metabolic rate after 30 days with this medicament was +9%, pulse rate 60 per minute, body weight 108 lb (49 kg), and blood pressure 210/70 mm Hg The serum cholesterol level had risen to 370 mm %, and angina pectoris again became frequent, requiring the repeated use of glyceryl trinitrate (see figure) It is to be noted that the basal metabolic rate, pulse rate, weight, and blood pressure were about the same on the two isomers, but with the sodium dextrothyroxine the serum cholesterol level was normal and angina pectoris did not occur, whereas with the sodium levothyroxine the cholesterol level was not controlled and recurrent angina pectoris was induced



Cessation of angina pectoris during substitution of dextrothyroxine for levothyroxine

It appears that the sodium dextrothyroxine administered to this patient is not contaminated with levothyroxine, even to the extent of 2 5% (0 1 mg in 4 0 mg) This experience indicates that sodium dextrothyroxine, indeed, has a qualitatively different physiology and biochemistry from sodium levothyroxine A basis for this difference is suggested by the work of Tapley,[3] which showed that after intravenous injection of similar amounts of the isomers in rats sodium dextrothyroxine became more concentrated in the liver than sodium levothyroxine, whereas the latter was found in higher concentration in the heart The possibility that sodium dextrothyroxine does not synergize with the catecholamines, as does sodium levothyroxine, is being investigated

The sodium dextrothyroxine was supplied as Dextroid and the sodium levothyroxine as Synthroid by Dr Thomas A Garrett of Baxter Laboratories Inc, Morton Grove, Ill

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THE DANGER OF BECOMING SATISFIED WITH STANDARDIZED TECHNIQUES —The technical excellence of a surgeon's art is important, for it is this quality more than any other that makes his operations safe and effective In the period of training it is an advantage for him to master the standard techniques so that they may become the scaffolding on which his surgical philosophy is built Yet there are dangers in perfecting techniques the dangers of becoming overly enamored of the craftsmanship involved and of being reluctant to adopt new methods The surgeon knows that employment of new techniques may, until they are mastered, result in a temporary increase in postoperative complications As a result of this knowledge his operations may become overstandardized The decision as to what operation should be performed may be made on the basis of what operation the surgeon does most expertly instead of what operation would be best for the patient When this happens and when a technique has become standardized too rigidly the operation may become a mere corollary to the diagnosis In such cases the reflex centers of the surgeon have taken control It is the hand that guides the mind —G Crile Jr, M D The Danger of Becoming Satisfied with Standardized Techniques *Surgery Gynecology & Obstetrics* July 1960

E. Vincent Askey, M.D., President, American Medical Association

"40 Million Get Checks From U.S. Treasury"

I was astounded to read recently that "we [the United States] already have reached the point where 40 million people—who with their families account for roughly half our total population—now receive checks from the national treasury."

This startling figure is given in an article, "How to Win a War," by Ed Lipscomb in *The Freeman* magazine. (I recommend the article on how we are losing at home our war to remain self-reliant, responsible individuals and to keep our nation a strong, anti-paternalistic state.)

Mr. Lipscomb contends, and I agree, that continued political domination of private and economic life is leading to voluntary surrender of freedoms for security insured by the government, an escape from personal responsibility and self-respect. Our national goal now seems to be a federal check in every mailbox and at least two civil servants for every citizen.

To me it is frightening that our nation is so indifferent to the trends toward national insolvency, toward the destruction of private incentive and toward perpetual programs of private life by public plan, as Mr. Lipscomb writes.

That we currently are working for national insolvency, there is no doubt. And we can expect to get what we seek.

Certainly we are promoting the destruction of incentive, and we can expect to reap what we sow.

Finally, we are piling on new and perpetual federal programs of more dollars for everyone, and we can expect the state to be "wet nurse" to all.

As each trend grows, our freedoms slowly come into Washington, and there is little likelihood of their return. Our money flows more rapidly into Washington, and only a fraction of it returns in any form whatsoever. This cannot be denied, and the great danger is that so few citizens and organizations are raising their voices in protest.

The feeling is abroad in the land that "nothing can stop it," "we might as well go along," and "what can one individual or one group do?" Our national interest concentrates itself on the Kremlin, the Congo, Cuba, and China because of our fears of communism and our desires for security.

Granted these matters are important, but are we not developing greater softness on the home front as we seek to build our strength against international communism? And in the long run is it not the lack of concern for solvency, the lack of incentive, and the lack of personal effort that may lead to our own national downfall?

When speakers and writers by the hundreds deplore our "glorification of mediocrity," when our national debt soars to 295 billion dollars and fixed obligations for future years reach 750 billion dollars, and when 40 million persons receive checks from the national treasury, can we deny that something has gone wrong?

As Mr. Lipscomb states, the war against these dangerous trends can only be won when as individuals we win our own personal war to take our side against these factors. Then we must support wholeheartedly the principles to counteract these self-defeating trends, practice daily what we believe, and help others win their personal wars.

The case of freedom is not an inevitable winner against tyranny and communism. We must show the world that our system is strong and solvent, produces intelligent and creative people, and is reliant upon dedicated individuals—not government—to build and promote the best way of life.

E. Vincent Askey M.D.

DEATHS

Abe, Tom, Los Angeles, St Louis University School of Medicine, 1934, certified by the National Board of Medical Examiners, associated with the Santa Monica (Calif) Hospital and the Culver City (Calif) Hospital, died June 17, aged 52, of ureteral carcinoma

Abrams, Michael Albert Ⓜ Baltimore, College of Physicians and Surgeons, Baltimore, 1909, served as medical head of his draft board during World Wars I and II, a member of the Baltimore Museum of Art and the Walters Art Gallery, served as a vice-president and board member of the Peale Museum, on the staffs of the Sinai and Mercy hospitals, died in Pikesville, Md , June 22, aged 75, of arteriosclerotic heart disease

Alsaker, Rasmus Larrsen, St Petersburg, Fla , Bennett Medical College, Chicago, 1910, died June 14, aged 77, of cerebral thrombosis

Barglow, David R Ⓜ Trinidad, Colo , Philipps-Universitat Medizinische Fakultat, Marburg, Prussia, Germany, 1934, Universita degli Studi di Roma, Facolta di Medicina e Chirurgia, Italy, 1936, interned at St Mary Hospital in Pueblo, member of the American Trudeau Society, accidentally drowned June 17, aged 53, while swimming in the Gulf of Mexico surf about 15 miles west of Panama City, Fla

Barnhart, Henry Byers, Pittsburgh, University of Pennsylvania Department of Medicine, Philadelphia, 1899, served on the staff of Ohio Valley Hospital in McKees Rocks, Pa , died June 15, aged 87, of acute congestive heart failure

Campbell, Robert Alexander, Whittier, Calif , University of Southern California College of Medicine, Los Angeles, 1894, Chicago Homeopathic Medical College, 1895, formerly member of the state board of medical examiners, served on the staff of the Clara Barton Hospital and later the Presbyterian Hospital–Olmsted Memorial, died June 23, aged 90, of pulmonary emboli and congestive heart failure

Carney, Thomas Bernard, Kewanee, Ill , Loyola University School of Medicine, Chicago, 1932, interned at the Hospital of St Anthony de Padua in Chicago, veteran of World War II, associated with the St Francis Hospital in Peoria and the St Francis and Kewanee Public hospitals, died July 10, aged 54, of coronary infarction

Davis, Louis, East Orange, N J , Long Island College Hospital, Brooklyn, 1919, staff treasurer and chief attending surgeon at St Michael's Hospital in Newark, where he was president of the staff in 1955-1956, fellow of the American College of Surgeons, died June 27, aged 64, of myocardial infarction

Smithwood, Robert Lowell Ⓜ Worthington, Ohio, Indiana University School of Medicine, Indianapolis, 1955, interned at the Indiana University Medical Center in Indianapolis, served a residency at the Caylor–Nickel Hospital in Bluffton, Ind , and the Harding Sanitarium in Worthington where he was a member of the staff, died in the University Hospital, Columbus, May 31, aged 35, of Hodgkin's disease

Trumper, Abraham, Montgomery, Ala , Jefferson Medical College of Philadelphia, 1911, specialist certified by the American Board of Pathology, died May 20, aged 71, of lymphocytic leukemia

Tucci, John Hugh, Brockton, Mass , born in New York City Aug 23, 1911, Middlesex College of Medicine and Surgery, Waltham, 1936, served on the faculty of Harvard Medical School in Boston, specialist certified by the American Board of Anesthesiology, member of the American Society of Anesthesiologists, Inc , secretary-treasurer of the Massachusetts Society of Anesthesiologists, anesthesiologist in charge of the Massachusetts Eye and Ear Infirmary in Boston, associated with the Morton Hospital in Taunton, chief of anesthesia at the Brockton Hospital, consultant in anesthesia at the Veterans Administration Hospital, died in the Brockton Hospital May 30, aged 48, of chronic pyelonephritis

Wolf, John Gibbon, Pueblo, Colo , University of Colorado School of Medicine, Denver, 1906, member of the American College of Chest Physicians and the American Trudeau Society, veteran of World War I, served with the city health department which he organized, associated with Parkview Episcopal Hospital and St Mary–Corwin Hospital, where he died June 10, aged 77, of cerebral hemorrhage

Woodworth, William P, Detroit, Detroit College of Medicine and Surgery, 1915, specialist certified by the American Board of Otolaryngology, member of the American Academy of Ophthalmology and Otolaryngology, at one time on the faculty of his alma mater, formerly secretary of the Wayne County Medical Society, veteran of the Spanish-American War, served on the staff of the Providence Hospital, died May 22, aged 78, of acute coronary attack

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Ⓜ Indicates Member of the American Medical Association

FOREIGN LETTERS

DENMARK

Lucofen for Adiposity—Mune and Pallese (*Ugesk laeger* [May 5] 1960) tested the weight-reducing action of Lucofen, an amphetamine derivative, on a series of patients and volunteers No toxic side effects were observed, but the weight reduction effected by it was significantly less than that effected by a placebo Questioned again after the drug had been discontinued for a month, none of the patients disclosed any craving for it, and most of them had maintained their weight reduction Indeed, some had lost even more weight in the interval The frequency with which the obese responded to the placebo tablets suggests that the nervous mechanism of weight reduction is of importance

Suicide Rates—At a meeting of the Danish Medical Society, Dr Grethe Paeregaard, Dr E Schiodt, and others (*Nord med* [May 19] 1960) discussed the reasons for Denmark's high suicide rate, which is almost three times that of Norway During the two world wars, which promoted national cohesion, suicide rates dropped, but there was a rise in the rate between these war On the whole the rate is about what it was 100 years ago, 22 per 100,000 per year Norway's relative immunity to suicides was traced by one speaker to the fact that only 15 to 17 per cent of its population lives in the country's capital, the relatively higher proportion living in rural areas, as compared with Denmark's 27 per cent Then there is the rate at which the two countries export their surplus populations from time to time, the exodus of emigrants rids the community of many of its potential suicides By the same token the communities welcoming immigrants find their hospitality rewarded by a rising suicide rate Yet another factor may be found in differences in the ethical standards of various communities, and in this connection one speaker suggested that the Danes were less religious than the Norwegians and for this reason were more prone to suicide

Hydroxychloroquine for Lupus Erythematosus.—Hydroxychloroquine was given by Dr B Sylvest (*Ugesk laeger* [May 26] 1960) to eight patients with lupus erythematosus and six with a polymorphic light rash All 14 patients had previously been treated with quinacrine and chloroquine which had been discontinued either because of side effects or because of no effective response to them The rash disappeared in seven and definitely improved in four others In the three remaining patients the drug was ineffective There were no significant side effects This treatment lasted from two weeks to eight months The usual daily dose of three to four tablets (600 to 800 mg) was lower than that given by Dr Brodthagen in 1959, his less encouraging results may have been due to a too large dosage

Diuretic Action of Bendrofluazide—Berthelsen and Eilersen (*Ugesk laeger* [May 12] 1960) compared the action of bendrofluazide with that of hydrochlorothiazide The 19 patients tested were suffering from dyspnea and edema of cardiac origin The dosage of bendrofluazide was 5 mg twice daily As with similar diuretics, long-term treatment with bendrofluazide showed a tendency to cause hypopotassemia, requiring a daily supplement of potassium chloride Animal tests have shown that the toxicity of the drug is slight

FRANCE

Deltacortisone for Cirrhosis—P Vesin (*Arch mal app digest* [Dec] 1959) reported the results obtained with delatcortisone therapy in 100 patients who had alcoholic cirrhosis with edema and ascites of varying degrees of severity The dose, given orally, was 40 mg the first day, 30 mg the second, and 20 mg from the third day on The duration of the treatment was 20 to 30 days for the patients who responded favorably The diet was kept balanced and moderately high in protein As contraindications the author listed renal lesions with azotemia and active peptic ulcer or a history of such an ulcer In 44% of the patients the ascites disappeared completely and did not recur after interruption of the treatment In 36% the treatment failed, and in 10% there was only temporary relief, with recurrence of the edema as soon as the treatment was abandoned

When the treatment was successful, the effect on the edema was rapid Diuresis began on the third or fourth day after the therapy was instituted, and the patients passed 2,000 cc or more of urine daily Edema and ascites regressed There was abundant elimination of sodium in the urine No significant hyponatremia was observed The patient's general condition improved, asthenia disappeared, and his appetite was regained In some patients a euphoric state was observed As to the biological effect, there was a decrease in potassemia since the elimination of potassium in the urine was increased The albumin-globulin ratio improved, and the level of cholesterol was frequently increased The treatment did not resolve the hepatic cirrhosis

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The items in these letters are contributed by regular correspondents in the various foreign countries

Purulent Meningitis in Children—C Sarrouy and co workers (*Pediatrie*, No 8, 1959) reported the results obtained in 66 children with purulent meningitis This disease affects mainly children under 1 year of age The most frequent infecting agents are Neisseria meningitidis and Hemophilus influenzae Escherichia coli are found mainly in children under 6 months of age Other germs such as Klebsiella pneumoniae, staphylococci, streptococci, and pneumococci are less frequently observed Clinical signs of purulent meningitis are vomiting, diarrhea, and crying Constipation is less common Neurological examination usually shows Kernig s and Brudzinski's signs, trismus, somnolence, restlessness, and, less often, coma or subcoma Tension of the fontanels and convulsions may also be present

These findings may be disguised under a digestive, hypotonic, or encephalic form, which makes an early diagnosis difficult if not impossible A lumbar puncture and an electroencephalogram should be made In 50% of the patients the encephalogram showed a normal tracing with slow dysrhythmia The spinal fluid contained many leukocytes, but at the beginning it might also be normal in spite of the presence of clinical meningeal syndrome In nine patients the albumin rate in the spinal fluid was above 300 mg per 100 cc, which meant a bad prognosis

Of the 66 patients 33 recovered Most of these were the older children with pure meningitis The mortality was higher among children under 6 months of age, with the highest rate among patients with meningitis caused by pneumococcus, Esch coli, and H influenzae

GERMANY

Anemia in Young Women—H Heller and coworkers of Berlin (*Ztschr ges inn Med*, no 24, 14 1105, 1959) recalled that Heilmeyer pointed out that chlorosis, or essential hypochromic anemia, which was thought extinct some years ago, is still being seen in young girls and has appeared to be increasing in frequency in recent years The condition is often associated with autonomic imbalance, its true nature is iron deficiency The causes of iron deficiency include heredity, extensive utilization of iron during growth, losses of iron during menstruation, diets poor in iron and vitamins, and disturbance of iron absorption

The authors observed for eight months 17 patients aged 15 to 22 years with essential hypochromic anemia The distinct greenish pallor pathognomonic of chlorosis was seen in only four patients Menstruation, which had been normal in all the patients in this series, receded in five with the appearance of anemia Hemorrhage, malnutrition, and focal infection could be excluded as causes Thrombocytosis, which is usually associated with this disease, was present in only two of the patients Gastric acidity was normal in nine, decreased in six, and absent in two Hemoglobin values ranged from 26 to 60%

Only the patients in whom no other disturbance was found were given supplemental iron Three with vitamin B_6 deficiency were at first given only this vitamin, and in two the blood findings markedly improved Combined treatment with iron preparations, vitamin B complex, and (in those with decreased gastric acidity) compound elixir of pepsin normalized the blood findings and iron level in all other patients, including two pregnant women The tryptophane test revealed a slight kynurenin increase in all patients It appears that the kynureninase system, which depends on vitamin B_6, was subjected to unusual stress in these patients so that the additional kynurenin formed under a tryptophane burden could not be fully broken down Two patients had a folic acid deficiency

UNITED KINGDOM

Fears Hit Potential Radiologists—Fears among students and their parents about the possible dangers of radiation are referred to by a Ministry of Health study group which has investigated the shortage of radiographers in the National Health Service The efficiency of hospital radiology departments has thus been seriously impaired Good publicity could counteract the sensational statements that appear periodically about radiation and could also explain the measures observed for protection of staff and patients In some areas the shortage is still due to lack of training facilities, but staffing was unsatisfactory even in areas with excellent facilities Commenting on the Ministry report, the *Lancet*, June 11, suggested that salaries and promotion prospects need to be improved, with substantial rises in the higher grades, if the quality of the service is to be maintained

New Journal—The new quarterly, *Journal of Child Psychology and Psychiatry*, is the official organ of the Association of Child Psychology and Psychiatry It will be primarily concerned with these subjects, but it is recognized that many other disciplines have an important contribution to make in furthering knowledge of the mental life and behavior of children, and relevant papers will accordingly be welcomed from such related fields as animal behavior, anthropology, education, family studies, pediatrics, physiology, and sociology The journal will be published by Pergamon Press Ltd, Headington Hill Hall, Oxford The annual subscription rates are to private individuals $15, and to libraries and institutions $20, a volume

BOOK REVIEWS

Postural Fitness: Significance and Variances. By Charles LeRoy Lowman, M.D., Sc.D., F.A.C.S., Director School, Physical Therapy, University of Southern California, Los Angeles, and Carl Haven Young, Ed.D., C.C.T., F.A.A.P.M.R., Professor of Physical Education, University of California, Los Angeles. Cloth. $7.50. Pp. 341, with 61 illustrations. Lea & Febiger, 600 Washington Sq., Philadelphia 6, 1960.

The authors believe that many disabilities and health problems have their roots in postural deviations. Consequently, they advocate a program of physical education in the schools that includes developmental activities designed to promote good posture and body mechanics. Postural fitness is defined as the capacity to maintain proper segmental relationships in all body movements. As such, it goes beyond sitting, standing, and walking to constitute the best body positioning for functional efficiency in any given activity.

The physician, physical educator, school nurse, parents, and others who may be involved are visualized as a team. Together, they can detect needs and plan programs of developmental activities for the child to help adjust irregularities in structural and functional postures. There are definite techniques for detecting such variations, tried procedures for approaching their alleviation, and exercise patterns of proved value to aid in their adjustment.

The authors take strong issue with those who contend that posture is a relative matter, essentially esthetic, with little connection to health. Rather, they maintain, structural deviations and poor body mechanics are a definite factor in such later ailments as sciatica, certain types of neuritis, bursitis, and arthritis. An athletic approach to physical education, particularly in the elementary and junior high school, they assert, will not fully meet developmental needs nor provide for the needs of all the pupils. In their opinion, too strenuous activity at an early age will result in joint injuries and damage to developing cartilages. These are not necessarily acute injuries such as strains, sprains, or fractures, but rather small repeated traumas that are cumulative in effect.

What is needed is a well-planned developmental exercise program applied to groups but keyed to the individual. A practical suggestion for doing this involves the grouping of pupils with similar developmental problems and the application of appropriate exercise programs with as much individual attention as possible. A completely individualized exercise program, they recognize, is hardly feasible in most schools and colleges. The authors make a good case for these points of view and the program they recommend. Their beliefs are based on years of experience in the fields of orthopedic exercise and physical education. Each has been responsible for the conduct of the kinds of programs they advocate for schools and colleges and various branches of the armed services. Yet, the practical implementation of their ideas on a widespread basis is unlikely.

Despite their logic, these concepts are difficult to get across to the general public. America is increasingly sports conscious and as a result our physical education programs are similarly oriented. Even activities for the handicapped tend toward adapted sports in most situations. Also, there is difficulty in obtaining the needed orthopedic consultation in many places as well as in finding physical educators prepared to carry out exercise prescriptions.

This book is, nevertheless, worthy of careful examination by physicians and physical educators who are interested in the fitness of youth. The recommended program also merits a trial run wherever available facilities and personnel make this possible. A worthwhile research project would be a comparative study of the long term results of a developmental program with those accruing from the type more commonly found in our schools and colleges.

FRED V. HEIN, Ph.D.

Arthritis and Allied Conditions: A Textbook of Rheumatology. Editor: Joseph Lee Hollander, M.D. Section editors: Edward W. Boland, M.D., and others. [First three editions written by Benard I. Comroe.] Sixth edition. Cloth. $20. Pp. 1306, with 417 illustrations. Lea & Febiger, 600 Washington Sq., Philadelphia 6, 1960.

Hollander and associates have brought up to date the sixth edition of this book published initially in 1940. In the intervening years this volume has been without a competitor in the conservative discussion of the diseases that manifest themselves clinically as arthritis or rheumatism. The first edition paid little heed to the group of diseases currently identified as collagen diseases or connective tissue disorders. Laboratory procedures for the diagnosis of rheumatoid arthritis were lacking. The steroids had not been discovered.

It is natural that rheumatoid arthritis, the articular disorder with the highest incidence of critical morbidity as well as incapacity, should be given a pre-eminent position in the volume. The "Etiology of Rheumatoid Arthritis" by Robinson discusses the possibility of hypersensitivity, the hereditary aspects, the psychosomatic factor, and the initial lesions The possibility that rheumatoid arthritis is an autoimmune malady is mentioned The listing of rheumatoid (ankylosing) spondylitis as a disease that resembles rheumatoid arthritis reflects the opinion of Boland that this malady is not a variant of rheumatoid arthritis This sentiment is not accepted by all experts in the field Similarly, Reiter s disease is discussed by Engleman under arthritis caused by or occurring with specific infection Others believe that Reiter's syndrome likewise is a variant of rheumatoid arthritis The diseases of the diffuse connective tissues, systemic lupus erythematosus, polyarteritis, and dermatomyositis are discussed by Schulman and Harvey who have contributed greatly to our understanding of these maladies 'Amyloidosis" by Calkins, 'Arthritis Associated with Blood Dyscrasias by Rodnan, and Hypertrophic Osteoarthritis" by Howell illustrate the diversity of discussion in the volume

The chapter on gout by Smyth was of particular interest to me Presumably this manuscript was submitted prior to the rediscovery that the kidney may participate in the dysfunction responsible for an increased concentration of uric acid in blood and body fluids In the paragraphs on treatment, insistence upon a low purine intake and avoidance of alcoholic beverages are not recommendations that are considered necessary in my experience The recommendation of administration of colchicine combined with a uricosuric agent, probenecid, is supported Furthermore, I would revise the introductory statement in the treatment of gout to convey the impression that modern therapy is more effective in this type of chronic joint disease than in any other type of articular disorder I would hope that the next edition would have clearer x-rays and photographs Improved techniques in reproduction should provide better illustrations for 1960 publications

Any critical comment should not be interpreted as disparaging This is an excellent book and remains the only comprehensive discussion of articular disorders in English The volume is a fitting accolade to the next president of the American Rheumatism Association

John H Talbott, M D

American Board of Legal Medicine, Inc Collected Papers 1956 1959 Cloth $10 Pp 238 Central Book Company, Inc, 850 De Kalb Ave, Brooklyn 21, N Y, 1960

The American Board of Legal Medicine was incorporated in 1951 Its membership is limited to doctors who also possess a degree in law or who have had at least five years' medicolegal experience Since its founding, this organization has sponsored a number of meetings This book represents a collection of papers presented at these meetings on a number of medicolegal subjects The papers themselves may be said to represent the expression of opinions of the men who have taken the time and trouble to present a point of view Individually, the papers are of uneven quality Collectively, they are of interest as they reflect the character of the sponsoring organization

Edwin J Holman

Medical, Surgical, and Gynecological Complications of Pregnancy By staff of Mount Sinai Hospital, New York City Edited by Alan F Guttmacher, M D, Obstetrician and Gynecologist-in-Chief, Mount Sinai Hospital, and Joseph J Rovinsky, M D, Assistant Attending Obstetrician and Gynecologist, Mount Sinai Hospital Cloth $16 50 Pp 619, with illustrations Williams & Wilkins Company, 428 E Preston St, Baltimore 2, 1960

This convenient sized book is printed in legible type on good paper Although it is the work of 68 collaborators, it is well-organized and well-written and has a detailed index

Believing in the existence of an exceptional interplay of medicine and surgery in obstetrics, the Mt Sinai Hospital departed from the usual pattern of organization when it opened its first department of obstetrics in November, 1952 It created 10 specialty clinics within the framework of the department of obstetrics cardiac, pulmonary, hypertensive, diabetic, hematologic, neurologic, psychosomatic, obstetric-gynecologic, endocrine, and vaginitis and varicose vein Each of the 10 special clinics meets in the prenatal clinic area at a different time than the ordinary antepartum clinic Members of the obstetric-gynecologic resident staff attend the special clinics for the dual purpose of their instruction and furnishing patients routine prenatal care This book is the result of the information gained by the participating group of nonobstetric specialists that staff these clinics It is not intended to replace any of the modern textbooks in obstetrics but rather to supplement them Following each chapter is a long list of modern references to supplement the text

The book covers the various systems such as cardiovascular, renal, and gastrointestinal and discusses surgical problems, collagen disorders, and genetic considerations Physiology, laboratory methods, and treatment are also dealt with Not only are the common problems included but also such rare ones as ptyalism, progressive infantile muscular atrophy (Werdnig-Hoffmann disease), pemphigus, rubella and fetal abnormalities, radiation in pregnancy, and cancer of the thyroid This is a concise, well-written volume which should be of inestimable value to obstetricians, general practitioners, and any doctors who counsel pregnant women

Byford F Heskett, M D

QUESTIONS AND ANSWERS

SWIMMING POOL CONTAMINATION

To THE EDITOR —1 *In what manner could flying bats with rabies contaminate a swimming pool? 2 In what manner could a dog in a swimming pool transmit worms to people?*

Elford Carpenter, M D, Greenville, S C

ANSWER —1 Although the transmission of infections of the upper respiratory tract, middle ear conjunctiva, skin, and digestive tract in public swimming pools is theoretically possible, proved occurrences of such transmission are rare If a rabid bat drank water from such a pool, and this in itself is most unlikely, some rabies virus from the bat's saliva might enter the water This could transmit rabies only if it were introduced into a deep (anaerobic) wound Such a chain of circumstances would be practically impossible

2 Intestinal worms or their ova from a dog could enter the water only if the dog defecated in the water—again an unlikely event Dogs and other animals are excluded from any well-run public swimming pool The fact that in such a pool the water is undergoing continuous filtration and recirculation or continuous change, and also continuous chlorination, is a further safeguard against disease transmission Exposure to air and sunlight also helps to destroy pathogens

HERNIATION OF NUCLEUS PULPOSUS

To THE EDITOR —*What is the etiology, symptomatology, therapy, and prognosis in patients with a displaced cervical disk?*

Samuel Barmak, M D, Nice, France

ANSWER —The question is understood to refer to the so-called "soft disk" This is a rupture of the posterior annulus fibrosus, with herniation of the nucleus pulposus Related topics, namely localized osteophytosis of the intervertebral foramen and cervical spondylosis, will not be discussed The soft nucleus pulposus ruptures through the posterolateral aspect of the annulus fibrosus and compresses either the nerve root alone or the spinal cord as well

The cause is obscure There are theories of developmental defects relative to the notochord and embryonic blood vessels There are metabolic theories of a continuing degenerative process with diminishing water content and elasticity of the disks, changes in the mucopolysaccharides and hyaluronic acids, or deficiency of vitamin C Trauma, usually indirect, is described in 30% of these patients as a precipitating factor

The symptoms depend on the direction in which the disk protrudes Most commonly it is lateral and affects only the nerve root and its blood vessels (and not the spinal cord) Early symptoms are pain in the back of the neck associated with pain radiating to the shoulder or arm The pain is aggravated by movements of the neck, coughing, sneezing, straining, and is usually worse at night It is worse when the head is flexed toward the affected side Examination reveals diminution of the normal cervical lordosis and limited range of movement of the neck The most common location is between the 6th and 7th cervical vertebrae where the 7th cervical root is compressed In this situation, pain is usually referred to the forearm There is paresthesia in the index and middle fingers, weakness of the triceps muscle, and diminution of the triceps reflex Objective signs of motor weakness and sensory changes are helpful in localization, but there are many variations and exceptions to individual findings as brought out by Yoss and associates (*Neurology* 7 673 [Oct] 1957)

When there is a ventrolateral protrusion of the disk, nerve root pressure and unilateral cord signs (usually a partial Brown-Séquard syndrome), occur With a midline rupture there is compression of the spinal cord with bilateral cord signs, with or without root pressure

Plain roentgenograms are helpful primarily in excluding congenital defects, certain neoplasms, trauma, and rheumatoid spondylitis In neurosurgical centers final preoperative diagnosis rests on myelography with iophendylate A summary of this technique is given in Spurling, R G "Lesions of Cervical Intervertebral Disc," Thomas, 1956

Conservative management includes bed rest for at least five days, fixation of the cervical spine with a collar, and traction with a head halter If there are no cord signs, conservative therapy should be practiced for at least two weeks If there is some relief of pain, it should be persisted in longer In general, the longer vigorous conservative measures are used, the better the results Surgical therapy is more urgent if the spinal cord is affected and if there is also a complete block in the spinal subarachnoid space on the jugular compression (Queckenstedt) test Spurling reported excellent response in 48% of 89 patients treated conservatively (with traction) and 74% of 45 of those treated surgically

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The answers here published have been prepared by competent authorities They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply Anonymous communications cannot be answered Every letter must contain the writer's name and address but these will be omitted on request

INTRAVENOUS INFUSIONS

To the Editor —*What occurs intravascularly during an infusion? Does a clot form about the needle and, if so, what is its eventual disposition?*

M D , Pennsylvania

Answer —No direct observations have been made on coagulation changes induced by introducing a needle into a human vein and allowing it to remain there It is known, however, that a "foreign" surface, which includes glass, steel, or other materials making up ordinary needles, presents to the blood a condition which releases Hageman factor from an inhibitor with which it is combined One of the first reactions in the coagulation sequence is thus initiated From in vivo observations on the circulation of the cheek pouch of hamsters (Fulton and Akers, *Fed Proc* 9 46, 1950, Lutz and associates *Circulation* 3 339, 1951), puncture of vessels by such needles results in prompt deposition on the endothelium of clumps of platelets These may adhere to the vessel wall, or they may be carried along in the blood stream to the lungs if the puncture is on the venous side of the circulation Such clumping reflects initiation or acceleration of coagulation which, if continued, results in fibrin deposition, with plugging of needle as well as vein, events which every physician has encountered

TOXOPLASMIC CHORIORETINITIS

To the Editor —*Patients who have had toxoplasmic chorioretinitis due to toxoplasmosis, verified by the skin test and the Sabin-Feldman dye test, have had their eye ailment healed Typical postinflammatory changes occurred, and the Sabin-Feldman test still showed positive results Are these patients to be treated further although the serologic test remains positive, even when clinical eye changes are not to be expected? Could a patient who made a clinical recovery from toxoplasmosis be given any assurance about future offspring?*

Max Goldschmidt, M D , New York

Answer —The initial diagnosis of toxoplasmic chorioretinitis in this group of patients is based on presumptive evidence as furnished by the dye test and the skin test In most areas of the United States, 20 to 40 per cent of the normal population over age 20 years have positive skin and dye tests The positive dye-test titer persists in these patients for many years and cannot be used as an indicator of activity of the disease Therefore, a positive dye test has no significance as far as activity of the eye disease is concerned If it and the skin test are positive in a patient with acute chorioretinitis, and if no other cause for the disease can be found one is justified in making a presumptive diagnosis of toxoplasmosis, and in treating it accordingly

After subsidence of the inflammation, therapy is not indicated even though the dye and skin tests remain positive, because it is known that any organisms which survive in the region of the infected area are in cysts and are not affected by therapy We have not encountered any cases in which a mother with presumptive acute toxoplasmic chorioretinitis transmitted the disease to her offspring, and there are no recorded cases of this type in the literature We have reported one case of a mother with undoubted congenital toxoplasmic chorioretinitis who gave birth to four children over a period of eight years Exacerbations of chorioretinitis occurred with the first and fourth pregnancies None of the offspring was infected, and all had negative dye tests after one year It seems fairly certain that the mother in this case will not transmit the disease to her offspring

"FASTING BLOOD CHEMISTRY"

To the Editor —*Are any of the usual or standard blood chemistry values, including serum electrolyte determinations, but not blood glucose determinations, significantly changed by the ingestion of an 'ordinary' breakfast? Must one consider, in the interpretation of laboratory reports of blood chemistry values, whether the blood was drawn before or after breakfast? With the ever-increasing number of blood specimens drawn from fasting patients for chemical determinations in a busy hospital, it is becoming more and more difficult to prevent a long delay in having some of the patients get their breakfasts Which values, if any, are significantly altered by the eating of breakfast?*

M D , New York

Answer —It is common practice to obtain blood specimens for chemical analysis after the patient has been without food for 12 hours, preferably in the morning before breakfast This procedure minimizes the influence of food ingestion and, in the case of hospitalized patients, of exercise and posture on the concentrations of various blood constituents Although it is reasonable to assume that standard conditions would tend to eliminate certain variables, little has been published regarding the effect of ordinary meals on the concentrations of the clinically important chemical constituents of the blood

Recently a study (Annino and Relman *Am J Clin Path* 31 155 [Feb] 1959) of the influence of an average breakfast on 15 frequently requested chemical determinations was made The determinations were of blood urea, nitrogen, glucose, carbon dioxide combining power, chloride, sodium, potassium, creatinine, total protein, albumin, globulin, cholesterol, calcium, phosphorus, and uric acid. With the exception of glucose and possibly phosphorus, an average breakfast did not affect any of the above constituents significantly in normal subjects. These authors concluded that, with these two exceptions, for screening or diagnostic purposes it is not necessary for patients to be in a fasting state when blood is drawn for the analyses listed above.

CHRONIC SINUSITIS

To the Editor:—*What are the necessary diagnostic procedures and treatment for chronic sinusitis with recurrent acute exacerbations due to coagulase-positive hemolytic* Staphylococcus aureus, *as shown in repeated cultures?*

Dale C. Hager, M.D., Beaumont, Texas.

Answer.—Regardless of the organisms involved, the diagnosis and treatment of chronic sinusitis is fundamentally the same. The diagnosis depends largely on the history, symptoms, physical findings, transillumination, x-ray studies, and diagnostic lavage.

Treatment depends on the location of the infection, the virulence of the organisms, and the resistance of the patient. It is customary to remove collections of pus by sinus irrigation after the acute congestion subsides. Failure of the sinus to respond to irrigation implies faulty drainage. Windows may overcome this deficiency, and this applies especially to the maxillary sinus. Between attacks, correction of drainage barriers is indicated. This sometimes requires submucous resection, infraction of an obstructing middle turbinate, removal of polyps, and an allergy study with management of the allergy when indicated. Instillations of medicaments in the sinuses are of questionable value, as is use of the antibiotics except during acute exacerbations with severe symptoms. External radical procedures are indicated only after all conservative measures have failed.

PREVENTIVE INOCULATIONS FOR TROPICAL RESIDENCE

To the Editor:—*The answer to the question "Preventive Inoculations for Tropical Residence" in* The Journal, *May 7, page 127, contains a statement to the effect that there are no drugs which will prevent an attack of malaria after a bite by an infected mosquito. It goes on to state that quinine or quinacrine hydrochloride will minimize the intensity of an infection or keep it subclinical.*

On the contrary, there are excellent drugs which will suppress almost all malaria, whether given before or after the infecting bite. Among these drugs are chloroquine phosphate and amodiaquine hydrochloride, and in uninterrupted weekly doses these drugs will continue to suppress almost all malarial infections. Furthermore, they will eradicate most Plasmodium falciparum infections, the exception being when infection occurs near the close of suppressive therapy. Malaria caused by Plasmodium vivax and Plasmodium malariae can be eradicated by a 14 day course of primaquine phosphate, given immediately after cessation of suppressive therapy on departure from the malarious area. There is cumulative evidence that primaquine in combination with chloroquine or amodiaquine will simultaneously suppress and eradicate all forms of malaria.

If the reference to quinine and quinacrine is an implied recommendation that these are the drugs of choice, there should be a qualifying statement that this is true only when chloroquine or amodiaquine are not available or are too expensive. The latter should rarely be true for a citizen of the United States.

Major Jerome H. Greenberg, M.D.
Department of the Army
Office of the Surgeon General
Washington 25, D. C.

To the Editor:—*The answer to the question "Preventive Inoculations for Tropical Residence" in* The Journal, *May 7, page 127, stated, "A person going from a temperate climate to Trinidad should be vaccinated against typhoid, paratyphoid, smallpox, and diphtheria. There are no other measures that have been proved valuable or necessary. . . . There is no active yellow fever in Trinidad."*

According to W. H. O. *reports, 15 cases of yellow fever, 2 of which were jungle yellow fever, occurred in Trinidad during the period 1951-1955. Two more were reported between 1958 and 1959. The U. S. P. H. S. booklet "Immunization Information for International Travel" recommends yellow fever vaccination for the interior, and the number of reported cases would seem to justify this recommendation.*

I would also like to quote from a letter published in the Lancet *(1:490 [Feb. 27] 1960) which is relevant to the question: "It is generally recognized that since the introduction of proguanil (paludrine), the greatest risk to which a European is exposed anywhere in the Tropics is paralytic poliomyelitis." It would seem wise, therefore, to emphasize adequate poliomyelitis immunization.*

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ABSTRACTS FROM THE LITERATURE

Archives of Neurology

3 121-222 (Aug) 1960

Inferences from Hypophysectomy on 450 Human Patients
B S Ray p 121
Neonatal Jaundice and Mental Retardation
W W Zuelzer p 127
*Motor Unit Action Potential Parameters in Human Newborn Infants—R J do Carmo p 136
*Intracranial Bleeding in Hemophilia
A Silverstein p 141
Basal Tegmental Self Stimulation After Septal Ablation in Rats
H P Ward p 158
*Observations on Selective Brain Cooling in Dogs
H Lourie and Others p 163
*Posterior Biparietal Ablations in Monkey
J A V Bates and G Ettlinger p 177
*Muscle Spindle Discharge and Ventrolateral Thalamic Stimulation—J Stern and A Ward Jr p 193
*Early Descriptions of Aphasia
A L Benton and R J Joynt p 205

Motor Unit Potentials in Newborn Infants —Normal data are necessary for electromyogram evaluation of infantile myopathies Motor unit potentials were recorded from quadriceps femoris and tibialis anticus muscles in 86 infants between 12 hours and 7 days old One hundred potentials from each muscle were recorded with concentric electrodes Polyphasic potentials had 9% incidence in quadriceps, and 16% in tibialis Mean amplitudes were 66% higher and durations about 20% shorter than comparable reported values in adults Cross-sectional motor unit dimensions between 2 and 10 mm were estimated with multi electrode recording in quadriceps

Observations On Selective Brain Cooling in Dogs —Our objective was to perfect a method for differential brain cooling and to study the effects of such cooling Forty dogs underwent cerebral cooling either by a jugular-carotid recirculating system or by simply cooling 1 carotid stream The latter method proved much safer The extracorporeal circuit consisted of a Sigmamotor pump heat exchanger and an oxygenator if needed In dogs, cooling 1 carotid effected rapid hypothermia of all cerebral structures Brain temperatures of 20° C (68° F) with rectal temperatures of 30° C (86° F) were reached in an average of 36 minutes At this point blood pressure averaged 30 to 50 mm Hg and pulse 30 per minute As cooling proceeded, intraocular and sagittal sinus pressures declined, the electrocorticogram slowed and flattened and often developed paroxysmal activity The cerebral A-V O and CO_2 differences fell during cooling but never reached zero even at brain temperature of 12 C (54° F)

Intracranial Bleeding in Hemophilia —A review of the records of 174 hemophiliacs who were admitted to the Mount Sinai Hospital, New York, revealed that 11 had probably experienced 1 or more episodes of intracranial bleeding (6 3%) Such bleeding was proven by lumbar puncture, craniotomy, or autopsy in 6 patients From over 85 cases of probable intracranial bleeding in hemophiliacs reported in the world literature, only 25 were found to satisfy rigid criteria for proof of both the diagnosis of hemophilia and the occurrence of intracranial hemorrhage The verified cases were analysed with respect to certain clinical features including the role of trauma, incidence of seizures, site of intracranial bleeding, and relation to prognosis lumbar puncture, and therapy On the basis of the data obtained, certain specific recommendations for the management of intracranial bleeding in hemophiliacs were offered

Posterior Biparietal Ablations in Monkeys —Four monkeys with bilateral posterior-parietal, 3 with bilateral inferior-temporal cortical ablations, and 4 without brain damage were compared for possible changes by means of neurological testing and quantitative behavioral tests In contrast to the other 2 groups the parietal operates were impaired in the accuracy of jumping and reaching, and they showed diminished spontaneous activity, their placing reactions were abnormal, they were impaired on the tactile and visual forms of 1 quantitative spatial discrimination test, and they were also impaired on tactile but not on visual, shape discrimination tests The temporal group was impaired on visual but not on tactile shape discrimination tests In the authors view certain but not all of the deficits in the parietal animals can be attributed to what we have called a selective motor retardation

Muscle Spindle Discharge —Lesions of the nucleus ventralis lateralis (V L) of the thalamus consistently result in improvement of parkinsonian symptoms Hassler postulated that paralysis of the gamma innervation of the muscle spindle is responsible for rigidity and akinesia We have studied the effects of V L stimulation upon the gamma system by monitoring the spindle afferent discharge from the contralateral gastrocnemius in the cat V L stimulation consistently produced gamma inhibition The integrity of motor cortex was necessary for this inhibition Globus pallidus stimulation similarly inhibited gamma function We have postulated that parkinsonian rigidity and akinesia result from an altered balance between the alpha and gamma system of the cord, with gamma inhibition its characteristic It follows that a lesion in V L or any other inhibitory structure e g , globus pallidus or motor cortex, might help restore this balance and relieve rigidity and akinesia

Early Descriptions of Aphasia —An analysis of the literature on aphasia from the Hippocratic writings to 1800 indicates that (1) Most of the clinical forms of aphasia had been described and certain common features of aphasic disorders had been noted However, sensory aphasia had not been recognized as a specific entity (2) It was known that aphasia could occur as a consequence of various diseases of the brain but no important ideas about localization had been advanced (3) The thesis that the basic psychopathology of aphasic disorders was an interruption in the connections between images or ideas and their linguistic signs

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Titles marked with an asterisk (*) are abstracted had been advanced (4) The outstanding early contributions were those of Johann Schmidt (1673) on alexia, Peter Rommel (1683) on motor aphasia, and Johann A P Gesner (1770) on jargon aphasia and the theory of aphasic disorders

Archives of Ophthalmology

64 167-291 (Aug) 1960

Papers Read at the 109th Annual Meeting of A M A, Miami Beach Fla June 1960

°Selection of Operative Procedures in Vertical Muscle Deviations
E A Dunlap p 167
°Vertical Recti Transplantation in the A and V Syndromes
J E Miller p 175
°Ultrasonography An Aid in Orbital Tumor Diagnosis
G Baum and I Greenwood p 180
Visual Field Studies After Temporal Lobectomy for Epilepsy
J P Wendland and S Nerenberg p 195
°Granuloma as Complication of Polyethylene Tube Buckling Procedures—H A Lincoff p 201
°Precancerous Epithelioma of the Limbus
F C Winter and T R Kleh p 208
Pathology of Ocular Leprosy
J H Allen and J L Byers p 216
°Electroretinography in Diagnosis of Visual Loss in Children
G Goodman and H Ripps p 221
°Ocular Study of Pulseless Disease
J L Dowling Jr and T R Smith p 236
Opsoclonus Ataxic Conjugate Movements of the Eyes
J L Smith and F B Walsh p 244
Contact Lenses for Aphakics
R C Welsh p 251
°Recent Experiences with Light Coagulation
H Wiesinger D Guerry III and W J Geeraets p 254
Surgical Treatment of Bullous Keratopathy
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°Peripheral iridectomy with Scleral Cautery
G S Tyner and others p 268
°Acute Complications from Present Day Corneal Contact Lenses
R K Lansche and R C Lee p 275
Surgical Treatment of Epithelial Cysts of Anterior Chamber
M J Hogan and E K Goodner p 286

Operative Procedures in Vertical Muscle Deviation—The choice of surgical procedures in ordinary vertical imbalances is now well delineated in accordance with established principles The A and V syndromes present an entirely different situation Surgical principles here are at present wholly unsettled This is due to varying concepts of their etiology There are 3 schools of thought, assigning the etiology either to dysfunction of (1) the horizontal recti, (2) the vertically acting muscles, or (3) a combination The author subscribes to this 3rd school Thus, depending on the school followed, the surgical approach varies markedly In addition to standard strengthening and weakening procedures on the muscles chosen there are the additional maneuvers of supra- or infraplacement of the horizontal recti insertions, and temporal or nasal displacement of the vertical recti insertions These are designed to increase or lessen further both primary and secondary functions The situation is further complicated at times by the co-existence of an unrelated vertical component

Vertical Recti Transplantation in A and V Syndromes—The A or V syndrome is a variation in the amount of esotropia or exotropia in up and down gaze Horizontal surgery usually resulted in correction of the strabismus in one position, but an overcorrection, undercorrection, or both, in other positions Transplantation of vertical recti in a horizontal direction resulted in correction or improvement of the syndrome Surgery has consisted of a symmetrical procedure on the horizontal recti for the minimal deviation, and a 7 mm transplantation of either the superior or inferior recti In V type exotropia the superior recti were moved nasally, temporally in A esotropia The inferior recti were placed nasally in A exotropia, temporally with V esotropia The average reduction of incomitance was 28 D, with no alteration in lid fissures, limitation of superior or inferior recti function, or marked hypertropia in 18 patients

Ultrasonography—Ultrasonography has been shown to be of great value in the management and diagnosis of orbital tumors In some cases this technique has been the only means of visualizing and locating the orbital lesion Lesions may be visualized with a resolving power of 0 02 mm in depth by 0 03 mm laterally The ultrasonographic appearance of the normal orbit is described as well as the pathological changes produced by orbital tumors Two cases of orbital hemangiomas are presented to demonstrate the practical application of this new technique

Granuloma and Polyethylene Tube Buckling Procedures—There have been 4 cases of intractable granuloma of the wound in 145 operations for retinal detachments The granulomas occurred only when an encircling polyethylene tube was implanted in the sclera Although the retina became attached the postoperative course of the eyes was complicated by a fleshy tumor growing from the wound, by burning, tearing and a mucopurulent discharge Conservative attempts to treat the granulomas failed It was necessary to reopen the wound and remove the polyethylene tubes The tubes were found to contain staphylococcus aureus which had been inaccessible to antibody and chemotherapeutic agents The granulomas grew from the ends of the infected tubes After the tubes were removed the eyes healed uneventfully

Precancerous Epithelioma of the Limbus—Carcinoma does not spring forth full grown from the conjunctiva, but is preceded by a period of gradual thickening and transition in the limbal epithelium In contrast to the uniformity of the individual cells in the normal epithelium, this transition period is marked by the development of great variation in the size, shape, arrangement, and staining reaction of both the cytoplasm and the nuclei The best name for all the various histologic types is precancerous epithelioma of the limbus The clinical and histologic characteristics of 24 cases were reviewed Complete local excision was found to be the treatment of choice, but a surprising recurrence rate (6 out of 15 cases) emphasizes the need for continued observation of these patients

Electroretinography and Visual Loss in Children—The differential diagnosis and prognosis of retinal anomalies, degenerations, atypical fundus pathology, and visual loss with normal fundi is a major problem in children where routine subjective tests may not be reliably employed *It is here that* the electroretinogram (ERG) is of greatest value to the ophthalmologist, neurologist, and pediatrician, since the ERG may be the most dependable and often the only means of assessing the extent of retinal damage In clinical electro*retinography the* retinal action potential to a flash of light is picked up at the patient s cornea by means of an electrode embedded in a contact lens The present paper discusses the use of electroretinography in the diagnosis of congenital tapetoretinal disorders and complete and incomplete forms of congenital cone blindness Though both disorders are due to retinal abnormalities, the absence of fundus lesions in many of these cases has led to frequent misdiagnoses and to instances in which the amblyopia was attributed to optic nerve or cerebral pathology

Ocular Study of Pulseless Disease—A case of pulseless disease was studied clinically and pathologically by various methods, including India Ink injection of the retinal vasculature A characteristic hypotensive retinopathy consisting of multiple micro-aneurysms, irregularly dilated veins with segmented blood flow, and decreased central retinal artery pressures measured by ophthalmodynamometry was delineated

Recent Experiences with Light Coagulation—The authors report on their experiences with light coagulation over the past 2 years They have found retinal tears, with or without early retinal detachment, to be the most important and favorable indication Thirty-four out of 36 cases treated were cured Small hemangiomas of the retina also showed excellent response, all of 5 eyes with this condition responded favorably to treatment. Large angiomas involving more than one fourth of the retina are less favorable, of 2 cases, one showed equivocal improvement, the other developed serious complications Prophylactic treatment of peripheral retinal degeneration is a controversial issue, but if one favors such, light coagulation offers the least traumatic approach The external applicator, using a convergent beam of light, can be employed successfully in the treatment of xanthelasmas In the formation of pupils, however, only moderate success was obtained by the authors Preliminary data on exposure times for the production of retinal burns were presented These indicate the expected dependence on fundus pigmentation

Peripheral Iridectomy with Scleral Cautery—This paper presents the results of peripheral iridectomy with scleral cautery performed on 42 eyes with various types of glaucoma In each case we believed that a filtering procedure and not a simple peripheral iridectomy was indicated Twenty eight were normotensively controlled An additional 6 were controlled with hypotony, 8 were uncontrolled The types of cases include 15 eyes with primary narrow-angle glaucoma believed to be in the synechial stage, 8 eyes with open angle glaucoma, 8 eyes with infantile glaucoma 5 eyes with juvenile glaucoma, and 6 eyes with secondary glaucoma The secondary group included an eye with Sturge Weber syndrome and another with Axenfeld syndrome The failures include 2 open angle glaucomas 3 infantile, 1 juvenile, and 2 of the secondary glaucomas

Complications from Present Day Contact Lenses—This study reports acute complications that have occurred from misuse and overuse of corneal contact lenses It is based on the treatment of 14 patients and a review of the literature Complications encountered were superficial punctate keratitis, confluent superficial erosion, full thickness epithelial abrasion, micro organismal infection of an abrasion with hypopyon, corneal edema, perforation of an ulcer, and endophthalmitis Complications resulted from building wearing time too rapidly, wearing lenses too long or irregularly or while asleep, and fitting with improper lenses Pathogenesis was due to the lens touching the corneal apex, strangulation of the cornea, foreign material lodging under the lens, micro-organisms infecting an abrasion, and inserting or removing lenses roughly Complications could have been prevented through close association of patient and technician with an ophthalmologist who would serve as captain of the team and be responsible for supervising, fitting, and following the patient

Archives of Pathology

70 133-268 (Aug) 1960

*Tobacco Induced Epithelial Proliferation in Human Subject
I Chapman and C H Redish p 133
*Pulmonary Vasculature of Children with Ventricular Septal Defect—H S Rosenberg and others p 141
*Method for Equating Age and Arteriosclerosis at Necropsy
S L Wilens and C M Plair p 149
*Ethyl Trichloracetate in Liver and Kidneys of Choline-Deficient Rats—G M Windrum and C C Kratzing p 156
*Serum Proteins Glycoproteins and Sialic Acid in Amyloidosis
D W Huestis and E A Jaeger p 168
*Submucous Fibrosis of Palate in Diet Preconditioned Wistar Rats—S M Sirsat and V R Khanolkar p 171
*Submucous Fibrosis of Palate
S M Sirsat and V R Khanolkar p 180
Studies of Skin Wounds in Rats Receiving Beta-Aminopropionitrile—G A Krikos and J L Orbison p 188
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Effects of Dietary Fats in Rabbits Fed Cholesterol
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Tobacco induced Epithelial Proliferation—There are multiple clinical observations to indict pipe smoke as a factor in causing stomatitis nicotina (a form of palatal leukoplakia) To determine the correlation of the amount of tobacco smoked and the number of years of smoking with the severity of the leukoplakia, we examined 19 patients with this disease Our studies showed that the total amount of tobacco smoked bore no relationship to the severity of the leukoplakia, but that the length of time smoking had continued showed a striking correlation 40 years exposure was the approximate dividing line between the slight to moderate (1+, 2+) and severe (3+, 4+) lesions To evaluate the possible contributory role of the heat of the smoke issuing from the pipe bit we evolved a simple method of measuring this temperature and showed that it is not a contributory factor

Equating Age and Arteriosclerosis at Necropsy—The aortas of 280 men, obtained at necropsy, were sorted according to age into half decades The aortas of each age group were arranged in sequence according to the degree of gross sclerotic change exhibited One from each age group showing the average degree of sclerosis for that group was selected and colored photographic transparencies, approximately life size, were prepared These served as standards for the average degree of aortic sclerosis found in each age group Subsequently all aortas examined at necropsy were compared to the standards and a chronological age was assigned to each one according to the degree of sclerosis present The procedure provides a simple and rapid method for determining whether arteriosclerosis is more or less severe in any aorta than in the average man of a particular age. A statistical evaluation of the age factor in arteriosclerosis was then carried out.

Pulmonary Vasculature and Ventricular Septal Defect.—The structure of the small muscular arteries of the lung of 52 children with ventricular septal defect was studied and compared with physiological data. The vessel measurements correlated roughly with the age of the patient in that there was a gradual thinning of the walls after the neonatal period. There was a marked overlap in distribution of size so that examination of a single vessel was found to be of little significance. There was very little direct correlation between the size of the medial layer of the small muscular arteries and such factors as pressure, shunt-ratios, resistance-ratios, or size of the ventricular septal defect.

Ethyl Trichloracetate in Liver and Kidneys.—Experiments were designed to see whether ethyl trichloracetate (ETCA) would prevent excess lipid accumulation in rat liver when given concurrently with a choline-deficient diet. It was found that 0.03 ml. ETCA per 100 Gm. of body weight lowered the liver lipid content of choline-deficient rats from 17.7% to 7% while rats with a choline-supplemented diet had 4% liver lipid content. There was an increase in the dry fat-free weight of the liver of rats receiving ETCA but only minor changes in liver water content. Histological evidence confirmed the beneficial effect of ETCA in the liver. However ETCA was unable to prevent the renal degeneration characteristic of choline deficiency and possibly ETCA may increase the tendency to renal damage.

Serum Proteins, Glycoproteins, Sialic Acid in Amyloidosis.—Widely differing results have been obtained in electrophoretic studies on the hyperglobulinemia of experimental and human amyloidosis. For this reason, we undertook to compare the status of the serum proteins in rabbits under 2 related sets of experimental conditions leading to amyloidosis, using a well-standardized and widely available paper electrophoresis procedure. Amyloidosis was induced by (1) ribonucleate injections, and (2) ribonucleate plus bovine serum albumin. We found an elevation of serum gamma globulin occurring at about the time of beginning amyloid deposition. This tended to return to normal as amyloidosis progressed. Our findings add some support to the concept that an increased circulating protein component may be deposited in amyloid disease. No significant abnormality in glycoproteins or sialic acid was discovered.

Submucous Fibrosis of Palate in Wistar Rats.—Submucous fibrosis of the palate is an important clinical condition in India. This paper represents an attempt at induction of submucous fibrosis of the palate in rats by local application of capsaicin, the active principle of chili. This arouses a limited connective-tissue response which is enhanced when the material acts on animals whose diet is deficient in protein or vitamin B. The microscopic changes (ordinary and electron microscopic preparations) observed in the collagen are identical with those found in human submucous fibrosis of the palate.

Submucous Fibrosis of the Palate.—Capsaicin produces a submucous fibrosis of the palate in rats. This paper is a study of ordinary and electron microscopic preparations of rats so treated and conditioned by desoxycorticosterone acetate. Of 16 treated animals, 12 showed elastotic degeneration of palatal collagen while all showed electron microscopic evidence of the degradation of palatal collagen into ill defined material. This is ascribed to a depolymerization by the hormone. Trauma to the palate in all probability is important. Treatment of the palate with desoxycorticosterone acetate influences the action of the local treatment by capsaicin.

Inflammatory Polyps of Ileum and Cecum.—Polyps composed of fibrous tissue disposed around and among blood vessels and infiltrated by inflammatory cells, predominantly eosinophils, have been reported in the stomach but not in the small intestine or colon, though similar lesions in these locations may have been called fibroma, angiofibroma, perithelioma, etc. Two cases of such inflammatory fibroid polyps, 1 of the ileum with intussusception, and 1 of the cecum with hemorrhage, have been observed. Both were successfully treated by surgical excision. The lesions appear to be inflammatory rather than neoplastic. They appear to be composed of granulation tissue of varying age and maturity and probably are sequelae of injury or irritation of the mucosa or submucosa of the gastrointestinal tract.

Primary and Metastatic Carcinoma of Liver.—During a 38-year period (1921-1958) 682 examples of advanced cirrhosis were encountered at necropsy at the Cincinnati General Hospital. The incidence of primary hepatic carcinoma in this group was 8.5%. Hepatoma occurred predominantly in post-hepatitic and post-necrotic cirrhosis (13 and 20%) and was uncommon in nutritional cirrhosis (1.2%). Cholangioma was rarely preceded by cirrhosis; concomitant cirrhosis, which occurred in 45%, was almost invariably of the biliary variety and could be attributed to the obstructive qualities of the bile duct neoplasm itself. Metastatic carcinoma was an infrequent complication of cirrhosis and had a lower incidence (4.2%) than in an equivalent group without cirrhosis at necropsy (10%). Obstructive cirrhosis constituted the most common form accompanying metastatic neoplasm. However, the cirrhosis was ordinarily a sequel of the initiating neoplasm itself which was often primary in the pancreas or biliary tract.

Human Aorta.—Injected heparin gives rise to changes in serum lipoproteins claimed to influence the development of atherosclerosis. Fifty inmates of an old-age hospital were kept on a continuous heparin treatment (10,000 I.U. twice weekly) until death (up to 4 years). The cholesterol content of the intima and media of the aorta was compared with the expected as known from normal human vessels. No difference could be found between the treated and the control group. Mortality and causes of death were the same as found in a control group of the same age and from the same hospital. In the dosage used the treatment with heparin had no influence on aortic atherosclerosis.

Penile Agenesis.—A study of the 27 reported cases of penile agenesis and 1 of our own was undertaken to further elucidate the embryology of the external genitalia and penile urethra. In the majority of cases the urethra ended on the perineum, but in 2 cases it pursued a normal course and was surrounded by erectile tissue, suggesting in the former cases a lack of genital tubercle formation and in the latter a secondary regression. None of the reported cases had an infra-abdominal wall defect, which would be expected if the genital tubercle and infra-abdominal wall were both formed from a band of caudal, migrating mesoderm as classically envisioned The perineal and scrotal raphe were present to a variable extent and did not correspond in extent with the urethrae The absence of significant scrotal abnormalities tends to substantiate the hypothesis that the labio scrotal swellings arise from outlying tissues and are not derived from the genital tubercle Penile agenesis was placed in the category of midline defects

Mucormycosis —Mucormycosis, a fungal disease usually caused by rhizopus, a normally non-pathogenic fungus, is reported from Natal, South Africa Twenty cases of the previously rare digestive-tract form and 2 involving the brain are described Cultures of Rhizopus stolonifer or Microsporum van Tiegh were obtained from 6 cases The disease occurred in debilitated patients, 7 cases showing the features of kwashiorkor None of the cases was associated with diabetes mellitus Secondary invasion of locally devitalized tissue, as in amoebiasis and typhoid, was suspected in some cases Other possible predisposing factors were acidosis, antibiotic therapy, and hypotension Infection of the digestive tract occurred by ingestion and further spread by continuity, contiguity, and via the blood stream Diagnosis in all cases was made post mortem, the dark haemorrhagic appearance of the lesions being very characteristic

Anesthesiology, Philadelphia

21.237-344 (May-June) 1960 Partial Index

Cytotoxic Properties of Anesthetics Tested in Cultured Epithelium
G Corssen and C R Allen p 237
Antisialogogue Effect of Phenothiazine Derviatives
A B Dobkin and D Palko p 260
*Caudal Obstetrical Anesthesia with 2 Chloroprocaine
C W Nellermoe and others p 269

Caudal Obstetrical Anesthesia with 2 Chloroprocaine —From January, 1958 through December, 1958 the authors used 2 chloroprocaine routinely for continuous caudal block in 1 030 obstetrical patients The technique used was the malleable needle method described by Moore There was evidence that the anesthesia was of low toxicity and of high diffusibility The maximum dose used was 4 9 Gm in a period of less than 1½ hours Satisfactory anesthesia failed to appear in 3 1% of the patients The onset of anesthesia occurred within 10 minutes in 88% of the remaining patients and in 30 minutes in the others The duration of anesthesia ranged from 55 to 90 minutes There were 132 complications (12 8%) observed in this series of 1,030 cases Nine (0 88%) were considered serious There were no fatalities or near fatalities in the series Two per cent solution of 2 chloroprocaine is now being used by the authors as the drug of choice for continuous caudal anesthesia

Archivio italiano di pediat e puericolt, Bologna

20 251-314 (no 4) 1960 Partial Index

*Lead Encephalopathy in an Infant
A Seganti and others p 251
Thrombocytopenic Purpura Associated with Eczema
M Midulla p 264

Lead Encephalopathy in an Infant —A 6 month-old infant is reported with severe symptoms of lead poisoning Inquiry into the source of the lead revealed the prolonged use of an ointment or lotion—containing lead—for the nipples by the mother The authors believe that the absorption of lead occurred through the nipples and was then excreted with the milk of the mother Symptomatic treatment and the intramuscular administration of calcium edetic acid (Ca EDTA) was rapidly followed by clinical improvement in the infant s condition, with significant urinary excretion of lead and concomitant diminution in porphyrinuria The authors call attention to the possibility that there might be a certain number of infants with subclinical forms of lead poisoning manifesting occult symptoms (anorexia, vomiting, pallor, etc) which stress the significance of the indiscriminate use of cosmetic lotions and ointments containing lead as an etiological factor Diagnosis of lead encephalopathy is not difficult provided one keeps this disease in mind, obtains roentgenograms of the long bones for evidence of heavy metal deposition, and performs urinary analysis for the presence of lead, thus preventing unpredictable complications

Australasian Annals of Medicine, Sydney

9 81-164 (May) 1960 Partial Index

Auto immunity in Human Thyroid Disease
I A Mackay and B T Perry p 84
Complement Fixation with Extract of Normal Thyroid in Serums of Patients with Thyroid Disease—E Hackett and others p 93
Precipitin Tests for Auto immunizing Thyroiditis
D Watson p 99
*Small-Bowel Biopsy with Suction Biopsy Tube
M Ralston I J Wood and A Hughes p 103
Gastric Ulcer Age Sex and a Curious Retrogression
B P Billington p 111
*Chronic Pyelonephritis and Hypertension
J F Gwynne p 150

Small-Bowel Suction Biopsy —The authors made minor alterations on the flexible suction biopsy tube, which Shiner of London had adapted for duodenal and jejunal biopsy from a gastric suction biopsy tube designed in their own unit in Melbourne In the present paper they report on 51 successful biopsies in 46 patients resulting from 74 attempts Fragments of jejunum were obtained in 38 and fragments of duodenum in 13 biopsies Eight representative cases and their corresponding biopsy findings are described, the conditions present including atrophic gastritis pernicious anemia and subacute combined degeneration of the cord with gastric atrophy, malabsorption with steatorrhea, and intestinal lipodystrophy (Whipple s disease) Pronounced jejunal atrophy was present in 2 cases of malabsorption, and the villi were distended with cells staining with the periodic acid-Schiff (PAS) method in the patient with intestinal lipodystrophy No constant major abnormality was found to be associated with atrophic gastritis or gastric atrophy The cause of both chronic atrophic gastritis and the malabsorption syndrome is unknown This lack of correlation between the histological changes in the stomach and small intestine in these 2 conditions suggests they have not a common causal factor The results obtained corroborate those obtained by Shiner and others that biopsy of the small bowel is neither distressing nor hazardous to the patient and is particularly valuable when the cause of intestinal malabsorption with steatorrhea, anemia loss of weight, vitamin deficiency or osteoporosis is being sought

Chronic Pyelonephritis and Hypertension —The author investigated the incidence of chronic pyelonephritis in autopsy studies on 200 hypertensive patients pointing out that one frequently uncovers primary renal disease in cases in which clinical investigation had failed to do so Chronic pyelonephritis is the commonest unsuspected renal disease in hypertensive patients, but sometimes it is not recognized or is mistaken for other causes of renal scarring The vague diagnosis of nephrosclerosis is made not infrequently when the classical features of chronic pyelonephritis are evident Histological evidence of chronic pyelonephritis was frequently found in kidneys showing a wide variety of gross appearances, it was found in 103 (51 5%) of the patients, being bilateral in 94 and unilateral in the others A study of the clinical records of these patients indicated that the renal disease was suspected or diagnosed in only 10% Essential hypertension was rare in young patients Malignant hypertension and uremia should suggest the presence of primary renal disease A causative relationship between hypertension and past infection could not be established in many cases A strong suspicion of such a connection exists in the younger age group but not in patients over 45 years of age when the incidence of essential hypertension increases The recognition of renal disease in a hypertensive patient is very important as treatment is always warranted The author recommends more thorough examination of the kidneys in hypertensive patients by roentgenoscopy and by cytological examination of the urine

Blood, New York

15 574-806 (May) 1960 Partial Index

°The Maturation Rate of Reticulocytes
M Baldini and I Pannacciulli p 614
Kinetics of Intravenously Injected Radioactive Vitamin B_1
E A Brody, S Estren and L R Wasserman p 646
°Hereditary Spherocytosis Hemolytic Mechanisms Iron Metabolism
W H Crosby and M E Conrad p 662
Characteristics of Penicillin Antibody
H H Fudenberg and J L German p 683
Hemorrhagic Thrombocythemia A Critical Review
F W Gunz p 706
Heparin Therapy in Autoimmune Hemolytic Anemia
W McFarland R G Galbraith and A Maile Jr p 741
Induction of Leukemia in Mice with Human Brain Extracts
S O Schwartz and others p 758

Maturation Rate of Reticulocytes—After release from the bone marrow the erythrocytes continue their maturation in the peripheral blood, the reticulocytes become mature erythrocytes The time necessary for the reticulum to disappear is the maturation time The author describes an in vitro culture technique for the study of reticulocyte maturation With the aid of this method it was shown that variations in the reticulocyte maturation in vitro paralleled similar variations present in vivo In studying the maturation of reticulocytes in patients with different types of anemia the author found that in the anemia of chronic uremia, in Cooley's anemia, and in pernicious anemia in relapse the maturation of reticulocytes was delayed not only because younger erythrocytes were present in the blood but also because the rate at which the reticulum substance disappeared was retarded A moderate delay in reticulocyte maturation was observed in a few cases of hereditary spherocytosis and of the hemolytic anemia that results from auto-immunization In patients with iron deficiency anemia or hemorrhagic anemia the maturation of the reticulocytes was always normal The number of reticulocytes in the peripheral blood is the result of 3 variables (1) the rate of output of reticulocytes from the bone marrow, (2) the degree of maturity at which the reticulocytes are delivered into the blood, and (3) the rate of disappearance of the reticulum substance There is reason to believe that defective maturation of reticulocytes in the peripheral blood indicates a similar defect in erythroblastic differentiation in the bone marrow The reticulocyte count in the peripheral blood is not a precise index of erythropoiesis

Hereditary Spherocytosis—The hemolytic disease associated with hereditary spherocytosis (HS) results from an incompatibility between the patient's abnormal erythrocytes and his spleen Abnormality of shape, disproportion between surface area and volume, increased fragility, the presence of increased amounts of non-hemoglobin iron (some siderocytes contain iron granules), a high mean corpuscular hemoglobin concentration, and an abnormality of dextrose metabolism are listed as abnormalities of the erythrocytes (spherocytes) of hereditary spherocytosis It is not known which of these abnormalities, if any, predisposes the spherocytes to destruction by the spleen The authors subjected 2 healthy young men with hereditary spherocytosis to repeated phlebotomies until iron deficiency developed and the erythrocytes became hypochromic The erythrocytes lost their spheroidal shape, became thin, and less fragile, but their life span did not increase Later, splenectomy corrected the hemolysis Prior to the experiment, the hemolytic disease in both patients had been compensated, that is, there was no anemia despite the rapid turnover of the erythrocytes In 1 of the patients, in whom the erythrocytes had a life span of only 5 days, the output of hemoglobin was computed to be as high as 135 Gm per day, or 20 times the normal rate The abnormal thickness and the fragility of the erythrocytes in hereditary spherocytosis do not appear to be responsible for the premature destruction by the spleen Iron deficiency corrects the spherocytosis, but it does not correct the hemolytic disease Splenectomy corrects the hemolytic disease, but it does not correct the spherocytosis

British Medical Journal, London

1 1379-1444 (May 7) 1960 Partial Index

°Rubella in Pregnancy
J E Gray p 1388
°Pure Red-cell Anemia and Thymoma
Z Freeman p 1390
°Steroid Arthropathy of the Hip
R Sweetnam, R M Mason, and R O Murray p 1392
Treatment of Polyarteritis Nodosa with Cortisone
G Pickering and others p 1399
Myocardial Infarction after Hemorrhage
K Davison and B J Smith p 1400
Epidemic Bronchiolitis in Infants
M E Disney and others p 1407

Rubella in Pregnancy—Six women had their pregnancy terminated because of rubella during the 1st trimester The method of termination was abdominal hysterotomy in 4 patients, vaginal hysterotomy in 1, and hysterectomy in 1 Three of the 6 fetuses had abnormalities in the ears, heart, and eyes, respectively There was also possible lesion of the lens in 1, and in 1 the lens was inadequate for examination It is suggested that the fetal lesions are the result of cell destruction following invasion by the rubella virus At the time of the infection the fetus is incapable of responding with an inflammatory reaction Although maternal antibodies penetrate the fetus, the intracellular virus is probably protected from them If the virus kill cells, it will be liberated and mopped up by circulating maternal antibodies, and concentrated foci of destruction may appear as simple absence of tissue If the hypothesis of virus survival is correct, it may be possible to recover the virus from affected lenses removed at operation, or even after death Another possibility is that the virus continues to survive in other, perhaps in many, tissue cells, for the mortality among babies affected by maternal rubella is unduly high

Pure Red Cell Anemia and Thymoma —A 74 year-old man complained of lassitude and loss of weight The hemoglobin level, initially of 6 1 Gm per cubic centimeter fell to 3 1 Gm in spite of the administration of 6 units of packed cells and intramuscular injections of iron As the hemoglobin level continued to fall, and in view of the reported success of thymectomy, the patient was operated on Section of an anterior mediastinal tumor which was easily removed showed it to be a spindle celled thymoma On the 7th postoperative day an iliac-crest biopsy was made the findings from this marrow sample combined with those from the peripheral blood were typical of erythroblast-hypoplasia The patient became febrile on the 14th postoperative day, his mental state deteriorated and he died in coma 4 days later Postmortem examination revealed that death had been caused by cerebral thrombosis The question of whether the thymoma is the cause of red-cell aplasia, or of whether both conditions are due to a common etiological agent has not been settled although there have been reports of cure following thymectomy and of cases in which the presence of the tumor preceded the development of anemia

Steroid Arthropathy of the Hip —Four patients, 3 with rheumatoid arthritis and 1 with pemphigus vulgaris, received continuous steroid therapy (cortisone hydrocortisone, prednisolone, and prednisone, respectively) for periods of 3 months to 2½ years In each patient the destruction of the femoral head, with consequent disorganization of the hip joint, was observed The outstanding feature of this condition was the relative absence of pain The hip disorganization was revealed in each patient by roentgenographic examination, and in each case the pattern differed from the bone changes which occur as a result of rheumatoid arthritis or osteoarthritis The pace of destruction in these 2 conditions soon slows down and the destruction seems to be limited by reactive new bone It is suggested that the corticosteroids have a damaging effect upon joints Careful observation of patients on a long-term or a high-dose steroid treatment is necessary in order to detect and treat early a painless hidden destruction which may occur in arthritic or even in previously normal hips The danger of this possible complication must be weighed against the benefit which the patient is likely to derive from the use of either oral or intra-articular administration of corticosteroids

Circulation, New York

21 643 802 (May) 1960 Partial Index

•High Serum Transaminase Activity in Heart Disease
T Killip III and M A Payne p 646
•Adrenocortical Steroids in Congestive Heart Failure
M A Greene A Gordon and A J Boltax p 661
•Coarctation of Pulmonary Artery Surgical Correction
W B Thrower W H Abelmann and D W Harken p 672
•Idiopathic Dilatation of Pulmonary Artery
M Deshmukh and others p 710

High Serum Transaminase Activity in Heart Disease —The authors recently observed a young man with advanced rheumatic heart disease and tight aortic stenosis in whom progressive hepatic dysfunction developed during his final illness and who showed a rise in serum glutamic oxalacetic transaminase (SGO-T) activity to 1,912 units Acute central necrosis of the liver was found at autopsy The authors reviewed the records of every patient in whom the SGO-T activity was greater than 500 units per milliliter per minute During a 30-month period 12,566 SGO-T determinations were made on 4,761 patients Most of the 157 patients in whom at least 1 SGO-T determination was above 500 units had liver disease, but 17 patients with high SGO-T levels had cardiac disease and no primary evidence of liver or biliary tract involvement Eleven of the 17 patients were admitted with acute myocardial infarction and 6 with severe heart failure Hypotension or shock developed in all 17, and in all but 1 right heart failure developed prior to high SGO-T activity Several patients had abnormalities of liver function when SGO-T activity was very high Eight patients died the autopsies showed histologic evidence of acute hepatic central necrosis In 4 there was necrosis of both heart and liver, in 4 necrosis of liver alone The authors conclude from these and from a control series of patients that very high SGO-T activity (more than 500 units) in patients with heart disease is, at least in part, caused by acute hepatic central necrosis secondary to a drop in cardiac output and reduced hepatic blood flow Caution is urged in the interpretation of increased SGO-T values as evidence for myocardial necrosis Acute circulatory changes may result in hepatic necrosis and increased blood enzyme activity without myocardial infarction

Adrenocortical Steroids in Congestive Heart Failure —The studies described were concerned with the effects of corticosteroids upon the clinical status, electrolyte balances, and cardiovascular dynamics in 9 patients with heart disease of various etiologies and congestive failure of varying severity A steady clinical state of 5 to 7 days duration was required as an initial control period Six of the 9 patients were studied for 13 to 16 days during the administration of prednisone and 3 patients during administration of triamcinolone, some patients were studied after steroid withdrawal Fluid balances were determined daily Catheterization of the right side of the heart and determinations of the blood volumes were performed prior to and at the termination of therapy In 5 patients increases in manifestations of heart failure and increased fluid retention occurred In 4 of them precarious clinical conditions requiring mercurial diuretics developed during steroid therapy In general, cardiodynamic status at the termination of steroid therapy correlated well with clinical status In 3 patients the clinical status did not change Some depression in urinary sodium and chloride excretions was noted during therapy These studies suggest that corticosteroids are generally detrimental in uncomplicated congestive heart failure Greater deterioration appeared in subjects having the more severe degrees of decompensation, suggesting that exogenous fluid-retaining influences were added to endogenous fluid-retaining forces, resulting in further accumulation of fluid in a circulatory system already burdened by hypervolemia

Coarctation of Pulmonary Artery —The authors recently observed 2 patients with stenosis of the main pulmonary artery They feel that the 1st patient had a rare form, as the constriction was in the middle third of the main pulmonary trunk The constriction was successfully treated by open operation and as such appears to be the 1st case treated definitively and studied with preoperative and postoperative cardiac catheterization There was also cinematographic documentation of the operation A plea is made for the routine use of open operation for correction of "pure pulmonic valvular stenosis" This allows better correction when the diagnosis is confirmed and flexibility for treatment if the unusual coarctation or constriction of the pulmonary artery is encountered

Idiopathic Dilatation of Pulmonary Artery—The 13 patients with idiopathic dilatation of the pulmonary artery were referred to the Bailey Thoracic Clinic, Philadelphia, for evaluation of their cardiac status They ranged in age from 3 to 35 years The clinical, roentgenologic, electrocardiographic, and hemodynamic findings are discussed Symptoms were either absent or mild A pulmonic systolic murmur was always present Roentgenoscopic studies showed various degrees of dilatation of the pulmonary artery in the presence of normal heart size The electrocardiogram was normal The hemodynamic studies showed a mild systolic pressure gradient across the pulmonic valve in some cases in the presence of normal right ventricular pressure The authors conclude that idiopathic dilatation of the pulmonary artery is a benign lesion and does not affect cardiac function to any appreciable degree Literature reports on 6 cases where autopsy was performed indicate that the patients died of unrelated diseases at ages ranging from 56 to 92

Gastroenterology, Baltimore

38 681-860 (May) 1960 Partial Index

°Hyperaldosteronism in Liver Disease
K S Henley D H P Streeten and H M Pollard p 681
Fluorescein String Test in Gastrointestinal Hemorrhage
W F Haynes Jr and F E Pittman p 690
Serum Leucine Aminopeptidase
E P Pineda and others p 698
°Leukocyte Function in Ulcerative Colitis
R J Priest J W Rebuck and G T Havey p 715
°Segmental (Ulcerative) Colitis
H Yarnis and B B Crohn p 721
Prednisone and Gastric Secretory Activity
I T Beck and others p 740
Follow-up of Patients with Stomal Ulcer
R S Boles Jr S F Marshall and R V Bersoux p 763

Hyperaldosteronism in Liver Disease—The authors report on 2 men and 2 women, 47 to 69 years of age, with cirrhosis of the liver who were admitted to the University of Michigan Hospital, Ann Arbor, and whose cases illustrated the role of hyperaldosteronism in the pathogenesis of refractory ascites due to the cirrhosis One of the 2 women lost her ascites after bilateral adrenalectomy and the 3 other patients had natriuresis and diuresis during the administration of the synthetic aldosterone antagonists SC 8109 and SC 9420 (Aldactone) together with chlorothiazide Both the synthetic aldosterone antagonists used are spironolactones It has been shown that the addition of a spironolactone in doses of 100 mg every 6 hours to a regimen of chlorothiazide (0 5 Gm twice a day) together with salt restriction (200 mg per day) and potassium supplements (3 Gm of potassium chloride per day) will relieve patients with cirrhosis of ascites which had failed to respond to the regimen without the spironolactones The urinary output of aldosterone is excessive in cirrhosis with ascites as well as in the presence of most other forms of abnormal fluid accumulation Since 1 of the most consistent effects of aldosterone is to promote renal retention of sodium, these observations suggest that hyperaldosteronism might be of some importance in the pathogenesis of abnormal fluid retention When hyperaldosteronism was overcome by bilateral adrenalectomy or by the use of certain spironolactones which antagonize the effects of aldosterone, loss of sodium and loss of ascitic fluid could be induced

Leukocyte Function in Ulcerative Colitis—The authors studied serial preparations of exudative cells from the skin of 19 patients with ulcerative colitis, using the technique of skin windows, in the Henry Ford Hospital, Detroit The basic pattern of exudation seen in normal control persons consisted of migration of phagocytic neutrophilic leukocytes and lymphocytes In 13 of the 19 patients the pattern of leukocytic exudation showed a difference from the basic normal pattern of exudation, namely, an excessive number of basophilic leukocytes The biochemical and pathogenetic implications of this qualitative defect of leukocytic function in patients with ulcerative colitis still need clarification

Segmental (Ulcerative) Colitis—The authors report on 63 male and 77 female patients, 3 to 65 years of age, with segmental colitis, the type of non-specific ulcerative colitis in which the more distal segments of the colon and also the rectum are free of the disease These 140 patients were observed for periods of up to 30 years It is recognized that a larger percentage of the cases of localized colitis are regional or right-sided in nature, and that many of these localized cases are pathologically probably granulomatous as well as ulcerative in nature Cases restricted to the right or proximal colon do not extend distally to the same extent as they were formerly believed to do There exists today, therefore, greater confidence in protracted medical therapy Not only is more time allowed for conservative observation, but also better-considered means of treatment, particularly the use of large if not massive doses of corticosteroids, offers a very promising field of therapy Of 71 patients treated surgically, 56 underwent ileosigmoidostomy with proximal colonic resection, this is the operation of choice, permanent relief of symptoms was obtained in 20 of 56 patients The longer period of follow-up, however, brings to light a higher percentage of late surgical disappointments, for which permanent ileostomy and total colectomy are the only means for the preservation of life and comfort of the patients For patients with extensive disease and those with complications and severe constitutional symptoms radical surgical intervention offers the 1 ultimate hope for restoration of efficiency and preservation of life

Journal Louisiana State Med Society, New Orleans

112 161-202 (May) 1960 Partial Index

°Transaminase Test
A M Hand and J W Wilson Jr p 161
Vaginal Fungi During Pregnancy
P J Krupp and M J St Romain p 176
Pigmented Moles
W J Perret p 183

Transaminase Test—The authors report on 87 patients studied for heart disease and 24 patients studied for liver disease, on whom serum glutamic oxalacetic transaminase (SGO-T) tests were performed at the Schumpert Memorial Sanitarium, Shreveport, La , during 1958 or January 1959 The results showed that the SGO-T test is of value in the study of patients with symptoms of coronary artery disease, especially in making a differential diagnosis on patients with a clinical picture compatible with myocardial infarction, but whose electrocardiographic tracings are not confirmatory

In these patients, serum transaminase values above 50 units aided in making the diagnosis of myocardial infarction, and values below 40 units were helpful in ruling out infarction when confusing clinical electrocardiograms were obtained Likewise, in patients suspected of having hepatic disease, high serum transaminase values were helpful in establishing the diagnosis, and normal levels aided in excluding hepatitis

Klinicheskaya Meditsina, Moscow

38 1-160 (May) 1960 Partial Index

*Prognosis of Polycythemia A A Lobanov	p 36
Oral Cavity in Primary Polycythemia in Radiophosphorus Therapy G F Senatorova	p 41
Radiophosphorus Therapy of Diseases of Peripheral Nervous System L I Levin	p 48
On the So Called Cardiac Pleurisy E I Likhtenshtein	p 50
Features of Bronchographic Examination in Bilateral Bronchiectasis Z I Levina and B N Bandalin	p 64

Prognosis of Polycythemia —On the basis of long-term observations of 16 patients with polycythemia, of whom 15 were treated with x-rays and radiophosphorus, and pertinent literature data the author arrived at the conclusion that radium therapy makes it possible to prevent thromboembolic complications, thus prolonging considerably the life and capacity for work of these patients By prolonging the life span, conditions are created for a more distinct manifestation of processes of anaplasia of hematopoietic organs with evolution into myeloblastic leukemia, which should be assessed as the true trend of the pathological process in polycythemia In a number of cases the possibility that the outcome of the polycythemia may be hypoplasia with anaplasia is not to be excluded When this occurs the debilitating effect of intensive erythropoiesis and the ionizing action of radiation should not be overlooked

Minerva ginecologica, Turin

12 307-346 (March 31) 1960 Partial Index

*Threatened Abortion and Premature Labor New Orientation U Ciulla	p 307
Ovarian Metastases from Mammary Carcinoma C Giomelli	p 314
Histaminolytic Activity and Radiotherapy in Women G P Balassi and F Blanda	p 330

Threatened Abortion and Premature Labor —An experimental treatment with 17 alpha-hydroxyprogesterone acetate (AP) and its methyl derivative 6 alpha-methyl-17-alpha-acetoxy-progesterone (MAP) was administered in 54 cases of theatened abortion and 49 of threatened premature labor Thirty-five patients with threat of abortion were treated with MAP and 19 with progesterone oil Of the 49 patients under threat of premature labor, 20 were treated with MAP and 29 with AP The maximal daily dose for either drug was 200 mg, and the duration of the treatment varied from 2 to 14 days The MAP therapy was successful in 31 of 35 patients with threat of abortion and in the 20 patients with threat of premature labor The AP therapy was successful in 17 of the 19 patients with threat of abortion and in 27 of the 29 patients with threat of premature labor These results indicate that the fundamental therapy in threat of interruption of pregnancy at any stage is progesterone and its derivatives with a higher progestational activity, among these 6 alpha-methyl-17-alpha acetoxyprogesterone (Luteocrin) is at present the most adequte luteoid Although both AP and MAP are useful in treating patients threatened with abortion, their main indication is for avoidance of premature labor because of the varied etiopathogenesis and the frequency of degenerative alteration in the ovum which occurs in spontaneous abortion

Nederlands tijdschrift v geneeskunde, Amsterdam

104 857-912 (April 30) 1960 Partial Index

Value of Fern Test in Cervical Mucus in Menstrual Disturbances K J H Verschoof	p 859
*Housing and Dry Rot in Etiology of Rheumatoid Arthritis H Varekamp	p 862
Audiometric Testing of Adolescent Students A G Dissevelt and others	p 869

Housing in Etiology of Rheumatoid Arthritis —The possible influence of the climate or of housing on the development or exacerbation of rheumatoid arthritis was investigated in the city of Leiden The houses inhabited by patients with rheumatoid arthritis were investigated particularly with regard to the presence of dry rot (caused by wood-decaying fungi) in the floors It was found that in a district of Leiden where dry rot is much more frequent the incidence of rheumatoid arthritis was higher than in other parts (72% of all houses, as against 11% elsewhere) Moreover in this district of poor housing more dry rot was present in the houses of rheumatoid arthritis patients than in a control group of houses No correlation could be established between the presence of rheumatoid arthritis and the dampness of houses

New England Journal of Medicine, Boston

262 1149-1200 (June 9) 1960 Partial Index

*Case Against Buerger s Thromboangitis Obliterans S Wessler and others	p 1149
Circulating Antibody in Penicillin Hypersensitivity Reactions A D Heggie	p 1160
Myocardial Infarction Associated with Pregnancy A Brown	p 1163

Case Against Buerger's Disease —Buerger, impressed by the presence of gangrene in young men found certain features which he believed to be characteristic of a distinct entity to which he applied the term thromboangitis obliterans The clinical picture was dominated by symptoms referable to recurrent progressive peripheral arterial insufficiency The lower extremities were involved more frequently than the arms and the ischemia often terminated in gangrene The disease was particularly common in young Jewish male smokers, superficial and deep phlebitis was frequent Skepticism concerning the identity of the disease has been expressed by a number of investigators The authors critically evaluated the nature of Buergers thromboangitis obliterans on the basis of data they obtained from different sources the clinical records of patients with peripheral arterial occlusive disease, the examination of amputated limbs, autopsy and biopsy material from young patients with beginning arterial insufficiency, from hearts and amputated legs studied by special injection and dissection techniques, and from venous biopsy material They arrived at the conclusion that the condition known as Buergers disease or thromboangitis obliterans is indistinguishable from atherosclerosis systemic embolization or peripheral thrombosis singly or in combination Although the special form of phlebitis described by

Buerger has been seen, the assumption that a specific arterial disease in association with a specific clinical syndrome exists when arterial obstruction is present in patients with this type of phlebitic reaction goes far beyond the available facts Thromboangiitis obliterans cannot be considered an entity in either the clinical or pathologic sense, and the term should be discarded

North Carolina Medical Journal, Winston-Salem

21 173-216 (May) 1960 Partial Index

*Surgical Treatment of Cerebral Ischemia
F H Taylor and others p 173

Surgical Treatment of Cerebral Ischemia—The authors report on 9 men (40 to 59 years of age), one 53-year-old woman and one 15-year-old boy with cerebral ischemia caused by extracranial vascular disease and particularly by occlusive disease of the internal carotid artery, who were operated on at the Charlotte Memorial Hospital, Charlotte, N C Contrary to the observations by other workers the right carotid system was involved as often as the left in these patients Endarterectomy was done in all patients except one who had repair of an arteriovenous fistula Five patients obtained good results or made a complete recovery up to 2 years postoperatively One of the improved patients died of an unrelated cause 1 year after endarterectomy, autopsy revealed a patent carotid bifurcation with smooth endothelium at the site of endarterectomy Three patients were not improved and 2 died In these unfavorable cases no backflow was obtained after endarterectomy was done These observations confirm the view held by many workers that cerebral ischemia can often be improved by direct surgical treatment of the extracranial vessels which supply blood to the brain

Policlinico (Surg Sect), Rome

67 67-132 (March-April) 1960

*Bronchiectasis and Electronic Microscopy
L Provenzale and S Rocca-Rossetti p 67

Bronchiectasis and Electronic Microscopy—The infrastructure of collagen bronchial fibrils from 47 bronchiectatic lungs was studied by electronic microscopy For comparative purposes 300 other electronic observations were computed and 23,000 other fibrils were studied In 20 of the 47 specimens the characteristic aspect of the collagen fibrils was deeply altered, while in the other 27 the structure and arrangement were normal These specimens were mostly from adults in whom bronchiectasis was secondary to stenosing peribronchial lymphadenitis The specimens with deep structural changes were from 11 adults and 9 children with no history of stenosis who had suffered from mild respiratory diseases In these specimens of bronchiectatic lungs with unknown etiological factor the collagen fibrils appeared thin, little-resistant to physical and chemical agents, and almost identical with those in the fetal stage This underdevelopment was observed not only in the area involved in bronchiectasis but also in healthy zones and adjacent lobes, and even in the contralateral lung It is considered as a systemic lesion of the bronchopulmonary tract which either permits a spontaneous and early development of bronchiectasis or constitutes the fundamental factor in producing the characteristic dilatations when other contributing elements are present These findings and the authors interpretation confirm the notion that in non-acquired bronchiectasis there is always a prenatal predisposition

Zeitschrift fur Kinderheilkunde, Berlin

84 1-124 (no 1) 1960 Partial Index

*Mortality of Fetal Erythroblastosis
W Neu p 23
*Fungi in Feces and Urine During Antibiotic Therapy
K Lang, and others p 69

Mortality of Fetal Erythroblastosis—The author reports on 59 girls and 51 boys who were treated for fetal erythroblastosis at the City Pediatric Clinic in Stuttgart, Germany, between 1947 and 1959 The mortality among these patients was reduced from 52% during the period of 1947 to 1954 to 2% during the period of 1957 to 1959, and the number of surviving children with cerebral damage was reduced from 21% to 2% The reasons for the improved results were the early diagnosis and quick transfer of the sick children to the pediatric clinic and treatment at the earliest possible moment The slowly performed exchange transfusion with citrated blood, repeated administration of calcium, and the addition of a pure heparin (Liquemin) prevent dangerous side-reactions The exchange transfusion removes the largest portion of the hemolytic blood of the patient and, with it, the increased serum bilirubin content and the antibodies This process may be supported effectively by the additional administration of a 6% solution of polyvinyl pyrrolidone in isotonic sodium chloride solution (Periston N), prednisolone and an antihistamine agent Penicillin prophylaxis reduces the risk of infection The improved methods of diagnosis make it possible for patients with milder cases of the disease to be subjected to treatment who would not have been treated in earlier days

Fungi in Feces and Urine During Antibiotic Therapy—Twenty-two children 14 months to 11 years of age, who were admitted to the Pediatric Clinic of the University in Bonn, Germany, were treated with antibiotics such as tetracycline, oxytetracycline, chloramphenicol, spiramycin or penicillin Mycologic examinations were made of urine and feces and of anal smears obtained from these patients for several days before the institution of antibiotic therapy and for several weeks in the course of therapy Similar examinations were made of specimens obtained from 26 adults More than 1,000 specimens were obtained from the 48 patients, those obtained before the institution of antibiotic therapy were negative in 85% of the patients, they became positive in the course of the therapy in 75% This applied not only to patients who received broad spectrum antibiotics by mouth, but also to those who were given medium spectrum antibiotics, and possibly also to those who received penicillin by mouth for longer periods Considerable amounts of fungi were observed in the feces of 2 patients who received tetracycline intravenously The additional administration of nystatin (*Mycostatin*) made the specimens negative in most of the patients The presence of fungi in the feces is to be considered as a preliminary stage of mycosis by which patients with diabetes mellitus, pregnant women, premature infants, and patients with malignant tumors, leukemia, and cachexia particularly are threatened In such patients prophylaxis of mycoses by oral administration of mycostatic drugs is indicated

SUBJECT INDEX

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A—Association
Coll—College
Commn—Commission
Comm—Committee
Conf—Conference
Cong—Congress
Dist—District
Div—Division
Found—Foundation
Hosp—Hospital
Indust—Industrial
Inst—Institute
Internat—International
M—Medical
Med—Medicine
Nat—National
Pharm—Pharmaceutical
Phys—Physicians
Soc—Society
Surg—Surgery
Surgs—Surgeons
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